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COMMON SENSE IN THE DIAGNOSTIC USE OF X-RAY

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The amount of exposure of a patient to ionizing radiation during diagnostic radiography was studied in a number of hospital patients. Measurements made on a wax phantom gave figures, in milliroentgens per film, for the dose of radiation received by the skin and by the gonads in various kinds of examination. Representative measurements on the phantom were then tested for accuracy by comparing them with corresponding measurements made on actual patients during examination of the urinary bladder and during pelvimetry. Agreement was sufficiently close to justify the continued use of the phantom for studies of exposure rates to ionizing radiation. The distinctions between one roentgen of local exposure and of whole-body radiation between irradiation of gonads and of the rest of the body and between somatic and genetic effects are emphasized. The danger of harm from the average diagnostic exposure to x-rays is insignificant compared with the danger of trying to practice medicine and surgery without their aid.

IONIZING radiation is a double-edged sword. It has power for good and is able to cause harm. These facts were known soon after the discovery of x-rays and radium. The development of our knowledge concerning the benefits of radiation will never end. Many more generations will pass before our knowledge of its harmful effects will be sufficient to control it properly. Until more exact data concerning proper and adequate control of radiation are available it is reasonable to over-control it.

One who is uninformed or partially informed concerning radiation might think that little has been done with regard to protection. Nothing could be further from the truth. Bythell and Barclay,[1] as long ago as 1912, said: "Stress must be laid once more upon the importance of avoiding any unnecessary exposure to the rays." This admonition was true then, and it is more important today. With the advent of the "Atomic Age" and the real possibility of exposing the entire population to dangerous levels of radiation, anyone responsible for any part of this radiation must have a good and adequate reason for its administration. By 1927 over 120 articles on the physics of protection had already been published. Rolleston,[2] this same year, indicated that the recommendations for protection should be based on the principles of absolute safety, and if we are to err we should err on the

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Read in the Symposium on Radiation Hazards before the Joint Meeting of the Section on Obstetrics and Gynecology and the Section on Radiology at the 107th Annual Meeting of the American Medical Association, San Francisco, June 24, 1958.

side of an excess in safety. Throughout the ensuing years most radiologists and many other physicians using radiation have made every reasonable effort to protect themselves, their personnel, and their patients from any unnecessary exposure. In 1957, the editor of *The Journal of the Faculty of Radiologists*[3] said that we should not think in terms of tolerance or maximum permissible dose but in terms of the "minimum possible dose."

If one studies the history of protection against radiation, there is no doubt that we have the knowledge to protect ourselves and others. It remains then for us to educate those who will voluntarily provide adequate protection against radiation and, if we must legislate, to pass sensible laws so that all who use radiation will comply with certain minimum standards. Extreme care must be taken so that those using radiation for industrial, agricultural, and other commercial purposes do not cut corners for economic reasons in providing protection. On the other hand, care must be taken so that those using radiation for medical purposes are not unduly restricted to the detriment of the patients.

Although we have been living in the nuclear age for several years now, it was not until 1956 that the public became alarmed about the hazards of radiation. This came about because of the sensational publicity given to the report of the National Research Council entitled "The Biological Effects of Atomic Radiation."[4] At about the same time a similar report of the British Medical Research Council, entitled "The Hazards to Man of Nuclear and Allied Radiations,"[5] was published. Much publicity was given to the dangers of atomic fallout. This undoubtedly was embarrassing to those responsible for atomic weapons testing. Even to this day a majority of the people of foreign nations want us to cease such testing of atomic weapons. With study it became apparent that the dosage received by the population at large and especially the gonadal dose from weapons testing was quite small by comparison to the dose received in using x-rays for diagnostic purposes.[4]

Medical x-rays then in a sense became the culprit, and many people refused to have necessary x-ray examinations. There is still a questioning attitude on the part of many patients regarding exposure to radiation. This adverse effect on the practice of medicine has come about because only one side of the story has been adequately told to the public by the lay press. Freedom of the press is a precious heritage which we must preserve. With this freedom go certain responsibilities.

Brucer[7] knows of at least 20 hospitals where they have stopped taking chest roentgenograms on admission. This is one segment of the population known to have a high incidence of positive findings. Knowledge of these findings helps to prevent spread of infections to hospital personnel and other patients.

It is possible to take chest roentgenograms with no demonstrable gonadal dose. According to the figures of Stanford and Vance[8] a female could have six chest films every day of her life to age 30 and a male could have one and each would receive less than 5 r to the gonads. This is half of the permissible dose to the gonads during this interval.

Last year numerous excellent publications in medical journals told the other side of the story, namely, the benefits of medical radiation. This attempt to weigh the benefits of radiation against its hazards has received little public notice. The impact on the public of telling the two stories is not equal even if equal space were devoted to both.

This public awareness of the dangers of radiation may become a good thing if every physician who has real knowledge concerning radiation would lose no opportunity to educate the lay public as well as fellow physicians concerning its benefits as well as the dangers. For over 30 years radiologists have imposed rigid rules on themselves insofar as protection is concerned. They have taken all reasonable measures to protect their personnel and patients, as well as anyone who may be in the vicinity of x-ray installations.

Radiation Dosage

The concept of dose insofar as radiation is concerned is a difficult one to encompass. The "roentgen" is the measure of exposure, and 1 r to a hand is vastly different from 1 r of total-body exposure. Anyone stating a dose of radiation, therefore, must indicate whether this is radiation to a part of the body, to the entire body, or to the gonadal tissue. Actually the dose that is most important insofar as the human species is concerned is that administered to the gonads. Ambiguity creeps in and ignorance is displayed if, in stating dosages, one does not make it crystal clear that total-body or partial-body exposures or skin or gonadal doses are being quoted.

A casual perusal of published data concerning radiation dosage to reproductive organs will show that certain x-ray examinations entail large gonadal doses. Stanford and Vance,[8] Binks,[9] and Martin[10] have shown that examinations involving the lower abdomen and pelvis, while representing a small percentage of examinations done in most offices and hospitals, account for a large percentage of the gonadal dose. We must recognize, however, that practically every x-ray examination contributes something to this gonadal dose. Diagnostic exposures are in general partial-body exposures. It would be the rare person who might receive enough radiation to cause even the slightest demonstrable body harm. Examinations where this might occur are calculated risks, just as are operative procedures, which patients agree to take. Many angiographic procedures require numerous x-ray exposures in two planes. Examinations of the gastrointestinal tract in which repeat fluoroscopies and radiographies are done are of vital importance to the patient's welfare, and, therefore, the doctor's judgment should prevail.

We have attempted to assay doses delivered to the skin surface and to the gonads to patients undergoing diagnostic radiographic examinations at Baylor Hospital, at Dallas, Texas. The gonad and skin doses were first measured on a plastic display manikin which had been fitted with sponge-rubber blocks to simulate lungs and then completely filled with paraffin wax. The ionization chambers used in making these measurements are known to have a depressed response for soft radiation, and for this reason some of the doses may be underestimated.

Table 1.—*Radiation Dose Received by Wax Phantom in Routine X-ray Diagnostic Examination*

Examination	Kv.	Ma.	Time, Sec.	Ma.-Sec.	F.F.D., In.	Added Filter, Mm. Al	Films, No.	Surface Dose/Film, Mr	Gonad Dose/Film (Female), Mr
Skull									
AP	75	100	0.5	50	36	2	2	700	0.4
Towne	75	100	0.5	50	36	2	2	700	0.15
Lateral	65	100	0.5	50	36	2	3	500	0.07
Chest									
PA	72	200	0.1	20	72	2	1	44	0.25
Lateral	84	200	0.1	20	72	2	1	65	0.65
Gallbladder									
AP	75	100	1	100	40	2	1	1,200	5
Oblique	75	100	1	100	40	2	1	1,300	6
Upper gastrointestinal series									
PA	65	200	0.5	100	40	2	1	450	20
AP (oblique)	70	200	0.6	120	40	2	2	630	24
PA (oblique)	70	200	0.6	120	40	2	2	630	20
Lateral	85	200	1.0	200	40	2	1	4,000	39
Spine									
Thoracic									
AP	75	100	0.3	30	40	2	1	370	6
Lateral	85	200	0.5	100	40	2	1	1,560	9
Cervical									
AP	65	100	0.5	50	40	2	1	250	8
AP	65	100	0.75	75	40	2	1	380	12
Oblique	85	100	0.2	20	72	2	2	55	0.6
Lateral	85	100	0.1	10	72	2	3	28	0.4
Lumbar									
AP	75	100	0.5	50	40	2	1	620	280
Oblique	75	100	0.75	75	40	2	2	930	350
Lateral	85	100	1.5	150	40	2	1	2,900	710
Lateral	85	100	2.5	250	40	2	1	3,900	1,500
Barium enema									
AP	80	200	0.3	60	40	2	1	840	230
PA	80	200	0.3	60	40	2	1	840	230
Oblique	80	200	0.5	100	40	2	2	1,400	380
Lateral	80	200	1.0	200	40	2	1	4,000	510
Drain	80	200	0.3	60	40	2	1	840	230
Pyelogram									
Kidney, ureter, bladder	70	100	0.75	75	40	2	1	860	260
5-min. film	70	100	0.75	75	40	2	1	860	260
15-min. film	70	100	0.75	75	40	2	1	860	260
Bladder	70	100	0.75	75	40	2	1	860	260
Bladder after voiding	70	100	0.75	75	40	2	1	860	260
Bladder									
AP	75	100	0.5	50	40	2	1	620	180
Transverse	85	200	2.5	500	40	2	1	9,700	2,500
Salpingogram									
AP	75	100	0.5	50	40	2	1	620	250
Oblique	75	100	0.75	75	40	2	2	920	340
Lateral	85	200	1.0	200	40	2	1	3,440	1,320
Pelvimetry									
AP	75	100	0.75	75	36	2	1	920	320
Lateral	85	200	1.0	200	36	2	1	3,440	1,320
Knee									
AP	70	100	0.2	20	40	2	1	230	0.5

It is hoped that in the near future this investigation can be repeated when ionization chambers of more uniform responses have been obtained. One who has not tried to make such measurements can hardly appreciate the difficulties encountered in trying to measure fractions of a milliroentgen delivered to a given area of the body.

These measured doses are given in table 1. The skin doses were then compared with those obtained by direct measurement on patients. The results of the comparison are shown in table 2. Finally the measured skin doses were compared with the values estimated from the known output of the x-ray unit, measured in milliroentgens per milliampere second at a distance of 100 cm. from the target for various combinations of operating voltage and filtration. The agreement between the estimated and measured values is reasonably close, and it is evident that the skin dose in any examination can be precalculated from a knowledge of the tube output, provided the target-skin distance is available.

Table 2.—*Comparison of Phantom Surface Dose with Patient Skin Dose*

Examination	View	Measured Skin Doses, Mr	
		Phantom	Patient
Bladder	AP	620	690
Pelvimetry	AP	920	1,160
	Lateral	3,440	7,200
	AP	920	780
	Lateral	3,440	2,340
	AP	920	3,270
	Lateral	3,440	3,270

Genetic Damage

It is well known that radiation can alter genes, the hereditary material contained in the chromosome. Geneticists agree that even the smallest dose of radiation may do some damage to the genes. They say also that, once damage is done, it is irreparable and the effects may accumulate over the years. The genetic mutations which occur are almost always undesirable when manifest in a living person. Those mutants resulting from x-ray exposure in species other than human beings show a decrease in longevity, an increased susceptibility to disease, and decreased fertility. Since the mutated genes are usually recessive, the first generation offspring do not manifest this genetic damage. This is the reason why geneticists are concerned about the human species 3 to 25 generations hence.

Mutations resulting from radiation are not different from those which have been occurring naturally in the human race for centuries. This naturally occurring rate of mutation is called "normal" for the human species. Geneticists have indicated that a gonadal dose to every living person of from 30 to 60 r would double this normal mutation rate. They fear that if this occurred it might be disastrous for the perpetuation of the human race. If such a dose should ever occur (60 rem) it certainly will not be from the medical use of radiation.

By present standards we are allowed a 14.3 r gonadal dose during the first 30 years of life; 4.3 r is said to come from natural background sources. Man has always lived with this. There are areas in the world, notably one in India, where the background radiation is much higher, and Prime Minister Nehru has indicated that there is no evidence of damage to these peoples, who have lived there for centuries. Up to the present time the fall-out from nuclear bomb explosions has contributed about 0.1 r gonadal dose. It is estimated that 4.6 r is given to the gonads from medical and dental sources.[10A] It is our opinion that, if we are considering the entire population of the United States, this figure is far too high. In any event several roentgens are still left for future increase in medical x-ray examinations before the drastically cut allowable amount will be reached.

The lay press, making sensational copy of such data, has presented this as a critical situation. Many of us who take the calculated occupational risk of working with radiation do not feel this sense of emergency. Whether these figures are accurate or not is unimportant, since the physician must use radiation when he needs it in the care of his patients. He must constantly keep in mind that he is to use the "minimum possible dose."

Some workers consider the somatic effects of radiation to be more important than the genetic effects. This seems illogical to us, since the human body is still a terminable unit while its genetic tissue is ostensibly immortal.

Importance of Roentgenography

If the use of radiation is to occupy its proper place in the practice of medicine, its hazards should be stressed to any physician who presumes to use it and its benefits should be stressed to the public. Every physician knows what an important tool the use of radiation is in both diagnosis and therapy. But few realize the magnitude of its importance. Several specialties in medicine would cease to exist as we know them today if the x-ray examination were not available. Radiology, of course, would be the first. Most all others would never have developed to their present status and would retrogress sharply if the use of radiation were taken from them.

Prof. Frederick Coller, at the University of Michigan, in an editorial entitled "The Debt of Surgery to Roentgenology,"[11] cited the work of Vesalius, Paré, Harvey, Hunter, Long, Pasteur, and Lister and stated that the discoveries of all of these great men did not make any significant impact on the care of patients insofar as improving surgery. He indicated that the fundamental reason for this was the fact that, prior to 1895 and the discovery of x-rays, physicians were not able to diagnose conditions which Hippocrates himself could not have diagnosed easily. He is in effect telling us something that all physicians know: intelligent therapy is based on accurate diagnosis.

The opportunity for curative surgery was limited until roentgenology developed. The development of much surgery in the future awaits better diagnosis, whether by x-ray or by other methods. Who will deny that the development of cardiovascular surgery to its present status could not have occurred without the aid of the x-ray examination? Besides angiography and angiocardiography as diagnostic aids, it is unlikely that cardiac catheterization can be performed adequately without the use of x-ray.

Comment

Modern life has many dangers, and most of these dangers are double-edged swords. Without fire our civilization would not exist, but it has power for harm as well as for good. The motor car has undoubtedly changed our entire civilization and yet at considerable cost in human life. Over 35,000 people are killed every year in automobile accidents, and this has been occurring for several years. This does not take into consideration the one million people who are injured. Many will become economic and medical liabilities for the rest of their lives. Property damage is enormous. Manufacturers continue to make automobiles larger, more powerful, and more lethal, but there is no clamor to adequately control the use of automobiles. Geneticists have done a good thing in calling our attention to the dangers of radiation to future generations. If their educational program were pursued with equal vigor in other fields, they could accomplish even more. Instruction in nonpropagation of known mental defectives is a good example.

None of these statements is made with the idea of minimizing the dangers of radiation or justifying the unnecessary use of radiation. Each physician should be concerned with keeping the medical dose of radiation as low as possible. His primary concern, however, is the health of his patients. Without preservation of the health of the present generation, there will be no future generation. In this connection the statisticians, if not the geneticists, might give us some information concerning the number of people who will not be born because accidents killed their potential parents. It would be interesting to project this through 25 generations.

The primary responsibility for the patient rests with that patient's physician.[12] Each physician must make himself aware of or be made aware of the dangers of somatic and gonadal irradiation.[13] If he does not need the x-ray examination for diagnosis or evaluation of progress of a disease, he should not request that this examination be done. This is particularly true if the physician's patient is a child, a pregnant woman, any woman in the childbearing period, or a man who is below the age of 40. The radiologist who understands the medical problem can keep the number of roentgenograms and the length of fluoroscopy to a minimum consistent with making a correct diagnosis. Radiation should be confined to the smallest possible area of the body in all examinations. Improperly performed examinations may give whole-body irradiation, and this should be avoided.

Keeping a permanent record of the amount of radiation each person receives does not seem feasible to us. Even if this could be done accurately it could not be a consideration in denying a patient an x-ray examination when the need is present. Here again the physician will have to determine the need for the examination and the patient will have to take the risk. One could not deny a craniotomy to a patient who may be dying of a meningioma simply because that patient has had a thyroidectomy, a laparotomy, and a thoracotomy. Neither could one deny this patient the necessary x-ray examination to localize the meningioma or subdural hematoma, even though his allowable dosage to somatic tissues or gonads had already been used.

Conclusions

X-rays used in medical diagnosis are not harmful; they are beneficial. This has needed to be said for several years.

It is the physician's responsibility, and indeed his prerogative, to use judgment in the application of any hazardous medical procedure to a human being. No one else should have this exclusive privilege. Any practitioner who uses radiation with conservative judgment and skill should not be made to feel uneasy about its use. The potentiality of causing damage to future generations should not prevent the real benefit to be obtained by the use of radiation in the present generation. The practitioner who uses common sense will view the current lay and scientific alarm about radiation dangers in its proper perspective. Data given to us by geneticists, radiation biologists, and physicists are important contributions to basic science and should be viewed in that perspective.

Those of us who work with radiation every day and who accept the occupational risks do not fear radiation but respect it.

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EXPOSURE TO RESPIRATORY DISEASE.—The public tend to have preconceived opinions about the effects of [commuting] on health. One of these is that travel, especially in the rush hour, predisposes to the spread of infections such as colds and influenza. That this may not be so is suggested by the experience of the Underground staff during the 1957 Asian influenza epidemic. Conductors who came in contact with the travelling public were little more affected than drivers. Moreover, bacterial counts in tube trains were considerably lower than those in offices and schools. Possible reasons for the comparative freedom from cross-infection include thorough ventilation, the traditional lack of conversation between strangers, and on theoretical grounds, exposure to small inoculating doses which serve to build up immunity. It is a pity that similar observations have not been made in suburban trains, where closed windows and dusty compartments must create quite a different set of circumstances. There still exists a need for the continued campaign against the unguarded cough and sneeze.—Travellers' Tales, *Medical World*, April, 1959.

RADIATION DOSAGE TO FEMALE GONADS DURING DIAGNOSTIC ROENTGENOGRAPHIC PROCEDURES

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There is, at present, no practical way to determine routinely the exact ovarian x-ray dosage delivered to each patient as she is examined. The greatest opportunity for reduction of such dosage lies in strict evaluation of the need for roentgenographic investigation of the gastrointestinal tract, the gallbladder, and the lumbar region of the spine in young women and of repeated roentgenographic examination in the handling of hip disease in young girls. Shields can be used to advantage to protect the ovary from the direct beam. Similar shielding can almost completely eliminate significant irradiation of the male gonads.

During recent years, a great deal has been written about the hazards involved in using x-rays to examine human beings for purposes of medical diagnosis. While many data have been accumulated, there is still considerable disagreement as to the interpretation of the data and it is not possible to define with any exactness the risk accepted when an individual patient is advised to have a particular x-ray examination. The time involved in determining the effects of small doses of radiation on persons and on their offspring is of necessity long, and it appears likely that scientists several generations from this one will have only a more nearly exact rather than an exact definition.

Nevertheless, on a number of points there is general agreement. Man cannot escape radiation. It is estimated that cosmic radiation and radiation from his surroundings produce a 30-year cumulative gonadal dose of 3 to 4.5 r. In a certain section of India, soil of unusual radioactivity may produce a 30-year cumulative dose of as much as 50 r in the gonads of inhabitants thereon. Incidentally, preliminary study of these persons shows no obvious evidence of somatic or genetic injury.[1]

As radiation is a part of the world in which man lives and as it constitutes a variable but ever-present part of his environment, to add something to this background dosage does not introduce a new element in his journey through life. Still, it is undesirable to exceed certain levels of radiation dosage. Such levels may be reached by a single large exposure or by the accumulation of multiple small exposures. When too much radiation reaches somatic tissue, the person may suffer in a variety of ways, such as the induction of the neoplastic process or the speeding up of degenerative processes. When too much reaches gonadal tissue, the patient's progeny may suffer, because radiation increases the mutation rate and the vast majority of mutations are undesirable.[2]

Until the danger levels can be determined accurately, a conservative course should be followed. In medical diagnosis, radiation should be used purposefully and the value of the information sought should outweigh the estimated hazard. If this principle is followed, the somatic hazard can be accepted as a calculated risk. In careful hands, it is less than many other hazards, medical and nonmedical, accepted daily without qualms—anesthesia, transfusion, automobile driving. The genetic hazard is another matter.

Estimation of hazard, at this point admittedly an educated guess only, involves consideration of the patient's age, the part of the body to be irradiated, and the approximate dosage to be delivered. The dosage can be held down by thoughtful planning of the examination and by painstaking technique.[3]

The Genetic Hazard

A combination of lack of information about the exact genetic effect of a given x-ray dosage and about the precise amount of gonadal radiation which people are now receiving causes difficulties. To weigh the value of medical information which can be obtained only by irradiating the gonads against the genetic hazard is not yet possible. But since it must be assumed that any dose of radiation, however small, can induce mutations, and since the genetic damage done by radiation is cumulative, particular attention must be paid to the amount of radiation absorbed by the gonads.[2b]

Studies have been done to determine gonadal dosage delivered in the course of diagnostic x-ray procedures.[4] A review of these studies shows that the male gonads receive a larger amount of scattered radiation during examinations in which they

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are at a distance from the direct beam of radiation than do the female gonads under the same circumstances. This is due to the protection afforded the ovaries by the thick pelvic tissues. Though the exteriorized position of the testes exposes them to scattered radiation, their location also makes it possible almost always to keep them out of the direct beam. Their location also makes it possible to reduce sharply the dosage from both direct and scattered radiation by the use of simple protective shields. By adding to other details of good technique the shielding of the testes during roentgenography of the lower abdomen, pelvis, and hips, significant irradiation of the male gonads can be almost completely eliminated.

Table 1.—*Ovary Dose per Exposure, in Milliroentgens*

	Stanford and Vance[5a] (1955)	Martin[5b] (1955)	Webster and Merrill[3a] (1957)			Present Study (1958)
			Adult	10-Yr. Old	3-Yr. Old	
Abdomen						
Low kv.	200		125	95	46	117
High kv.						74
Gallbladder	5.2	90	2-3			9* 6†
Gastrointestinal						
Anteroposterior	9	150	50	95	48	22
Oblique	9		70			34
Lateral			60			
Barium enema						
Anteroposterior	20		190	110	48	154
Oblique			250			
Lateral			280			
Lumbar spine						
Low kv.						
Anteroposterior	227	50	150	65	50	304
Lateral	86	150	240	180	110	58‡
High kv.						
Anteroposterior	40					
Lateral	16					
Pelvis	210	300	115	50	50	245
Lumbosacral (lateral)	800	500				418‡ 253§
Hip						
Anteroposterior						236‡ 52§
Lateral			410	150	50	
In pregnancy						
Abdomen						
Low kv.	260	1,500				220
Lateral						557‡ 345§
Pelvis						1,077‡ 489§

* Right ovary.
† Left ovary.
‡ Ovary nearer source.
§ Ovary farther from source.

The position of the ovaries protects them from scattered radiation when they are at a distance from the beam, but, on the other hand, it requires them to be in or very close to the direct beam during a variety of diagnostic procedures involving the roentgenographic or fluoroscopic visualization of structures in the abdomen, pelvis, and hips. For this reason the importance of cones and shields in holding down the ovary dose can hardly be overemphasized. When an ovary is in the direct beam of a large or round cone but outside the beam of a smaller or rectangular one, use of the latter involves an ovary dose about one-tenth that received in the direct beam. Increasing the distance of the ovary from the edge of the beam reduces its dosage more effectively than high-kilovoltage technique or added filtration. An increase in distance of 2 in. decreases the ovary dose by a factor of three. The use of a continuously variable rectangular diaphragm has been recommended as the best way to take full advantage of the control of scattered dosage by accurate centering in fields of minimal size.

Because of the relative unimportance of the somatic hazard and the ease of avoiding testicular exposure, in the well-run department of radiology concern about the genetic hazards of roentgen diagnosis can be focused on a limited number of procedures in which the beam of radiation must be passed through or near the ovaries of female patients still within the child-bearing age.

Ovary Doses

Review of those portions of some of the studies to determine gonadal dosage[5] during diagnostic x-ray procedures which deal with these examinations in females shows a wide range of figures (tables 1 and 2). Our own values were obtained from an adult female cadaver of average development, nutrition, and physique. The external measurements of the pelvis were 19.75 cm. in the anteroposterior dimension and 33 cm. in the transverse dimension. Baldwin Farmer type BD-11 ionization chambers were placed against the ovaries through a Pfannensteil incision. Techniques then in current use in our laboratory produced the figures noted, as read on a Farmer portable electrometer, Type R. B. Mk. 5, and corrected for temperature and barometric pressure.

Table 2.—*Ovary Dose per Examination, in Milliroentgens*

	Stanford and Vance[5a] (1955)		Martin[5b] (1955)	British Medical Research Council[5d] (1956)	Present Study* (1958)
	Hospital A	Hospital B			
Abdomen	700	740	203	200	234
Retrograde pyelography			803	1,290	234
Intravenous pyelography	2,320	1,030	1,360		468
Cholecystogram	4.7	0	378	15.6	52
Barium meal	22.5	18	360	9	241
Barium enema	12	6	520	20	616
Lumbar spine				713	780†
Lumbar spine and sacroiliac joint	1,585	1,515			
Lumbosacral joint			1,025		
Sacroiliac joint				713	722†
Pelvis	294	357	800	210	245
Hip	420	273	440	210	481
Pelvimetry	535	2,140		1,280	1,517

* Fluoroscopy dosage not measured.
† Ovary nearer source.

The wide range emphasizes the opportunity for control of ovary dosage by careful selection of equipment and technique and by thoughtful planning of procedures. It also points up the fact that equipment, technique, and procedure are not standardized but are varied from department to department by individual radiologists. Finally, it must be remembered that, even in the same department, variations in human physique make ovary dose measurements in one patient inapplicable to the next patient. There is, at present, no practical way to determine, as a matter of routine, the exact ovary dosage delivered to each patient as she is examined. Nevertheless, the available data permit a close enough estimate for clinical guidance.

Badly needed at this point is information which will permit a fairly exact idea of how many roentgenographic examinations of women within their reproductive years are being done which involve direct irradiation of the ovaries or indirect irradiation from a nearby beam. As a contribution to that end, the number and age distribution of such examinations done in the department of radiology of the University of Virginia Hospital at Charlottesville in 1957 were determined (table 3). The institution is a 485-bed general hospital. In 1957, there were 15,521 admissions, 81,419 visits to the nonprivate outpatient department, and an estimated 70,000 visits to the private offices in the medical center. In the x-ray department, 44,302 diagnostic roentgenographic procedures were performed.

TABLE 3.—*Age Distribution of Roentgenographic Procedures Involving Significant Ovarian Dosage, University of Virginia Hospital, 1957*

	Age, Yr.										Subtotals*					
	0-5		6-15		16-25		26-35		36-45		<46		>45			Estimated Av. Dose (Adult) per Examination, Mr.
	No.	%	No.	%	No.	%	No.	%	No.	%	No.	%	No.	%	Total No.	
Abdomen	31	10.4	20	6.7	81	27.3	89	29.8	77	25.8	298	43.0	394	57.0	692	234
Kidney, ureter, and bladder	2	1.5	8	6.0	30	22.6	45	33.8	48	36.1	133	40.0	200	60.0	333	234
Retrograde pyelography and cystography	10	13.9	8	11.1	14	19.4	12	16.7	28	38.9	72	39.0	112	61.0	184	234
Intravenous pyelography	12	4.2	33	11.4	52	18.1	89	30.9	102	35.4	288	54.0	241	46.0	529	468
Gallbladder	1	0.3	10	3.2	54	17.1	107	34.0	143	45.4	315	44.0	394	56.0	709	52
Cholangiography	1	5.3	3	15.8	2	10.5	4	21.0	9	47.4	19	51.0	18	49.0	37	52
Gastrointestinal	15	3.2	19	4.1	82	17.7	143	30.8	205	44.2	464	46.0	551	54.0	1,015	241
Small intestine	3	8.8	5	14.7	5	14.7	9	26.5	12	35.3	34	49.0	36	51.0	70	616
Barium enema	8	2.2	19	5.2	36	9.9	106	29.2	193	53.3	362	45.0	442	55.0	804	616
Pelvimetry	0	0.0	7	6.3	78	70.3	21	18.9	5	4.5	111	100.0	0	0.0	111	245
Placentography	0	0.0	29	9.1	213	66.8	67	21.0	10	3.1	319	99.7	1	0.3	320	777
Salpingography	0	0.0	0	0.0	31	40.3	40	51.9	6	7.8	77	100.0	0	0.0	77	322
Fetal	0	0.0	6	10.0	19	31.7	26	43.3	9	15.0	60	100.0	0	0.0	60	777
Lumbar spine	18	4.2	34	7.9	80	18.8	135	31.5	161	37.6	428	49.0	432	51.0	860	780
Pelvis, coccyx	33	15.4	18	8.4	45	21.0	50	23.4	68	31.8	214	52.0	198	48.0	412	245
Hip	66	37.1	34	19.1	24	13.5	20	11.2	34	19.1	178	40.0	263	60.0	441	481
Lumbar myelography	0	0.0	0	0.0	5	11.9	13	30.9	24	57.2	42	54.0	36	46.0	78	780
Totals	200	5.9	253	7.4	851	24.9	976	28.6	1,134	33.2	3,414	50.7	3,318	49.3	6,732	

* No of patients under 46, 1,976 (55%); over 45, 1,599 (45%); total, 3,575. Examinations per patient under 46, 1.73; over 45, 2.07.

Several points should be noted. No attempt has been made to estimate the ovarian dosage delivered by fluoroscopy incident to the examinations in question. In the examination of children, the younger and smaller the subject the closer the ovaries come to the x-ray beam in examination of parts outside the abdomen and pelvis. Significant dosage is delivered to children's ovaries by procedures other than those listed in table 3. The estimated average ovary dose per examination applies to adults only. The number of placentograms taken during the period selected was abnormally large because of an experimental program approved by the Atomic Energy Commission (AEC) in the department of obstetrics.

X-ray examinations which involve irradiation of the pregnant uterus usually involve direct irradiation of the fetal gonads. It has been estimated[5b] that the gonads of a male fetus in a vertex presentation may receive from 2 to 4 rads during roentgenography of the pregnant uterus.[6] A number of factors combine to indicate particular caution in subjecting the pregnant uterus to roentgenographic examination. The thickness and volume of the part necessitate heavy exposure for adequate penetration. The maternal gonads must be exposed, the fetal gonads must usually be exposed, and often the entire fetus must be irradiated. It is clear that during pregnancy only essential roentgenographic procedures should be performed. In fact, the peculiar hazards involved in irradiation of the fetus led the Russells[7] to go as far as to recommend that elective roentgenography of the pelvis in females within the child-bearing age be done in the two weeks after the last menstrual period in order to avoid irradiation of an unsuspected pregnancy.

In our laboratory, 55% of the female patients who underwent roentgenographic procedures involving significant absorption of radiation in the ovaries were under 46 years of age. Because these patients had a somewhat lower number of these procedures per individual patient (average 1.73 against 2.07), they received 50.7% of the examinations rather than 55%.

The genetic significance of this radiation is uncertain, but our experience indicates that, assuming only essential examinations are performed during pregnancy, the greatest opportunities for reducing ovarian dosage lie in strict evaluation of the need for roentgenographic investigation of the gastrointestinal tract, the gallbladder, and the lumbar spine in young women and of repeated roentgenograms in the handling of hip disease in young girls. In regard to serial studies of hip disease, round shields can easily be placed on the abdomen over the ovaries to protect them from the direct beam without obscuring the field of interest. The younger and smaller the subject, the easier it is to place shields accurately, but, with care, the ovaries of adults can be shielded in this way. This measure can be used to advantage not only in the examination of the hip but wherever shields can be placed over the ovaries without concealing structures which need to be visualized.

Summary

Our current state of knowledge about radiation hazards and ways to minimize dosage during medical diagnostic roentgenography makes it possible to focus our concern on those procedures which involve passing the x-ray beam through or near the ovaries of women not past the child-bearing age. Statistics from the University of Virginia Hospital at Charlottesville showed (1) the number of roentgenographic examinations done in 1957 which involved delivery of relatively large radiation dosage to the ovaries, (2) the age distribution of the patients undergoing these procedures, and (3) an estimate of the average radiation dosage, exclusive of fluoroscopy, delivered to the ovaries of adults by the techniques then in use. Assuming that only essential examinations will be performed during pregnancy, the greatest opportunity for ovarian dosage reduction in this particular institution lies in strict evaluation of the need for roentgenographic investigation of the gastrointestinal tract, gallbladder, and lumbar area of spine in young women and of repeated roentgenographic examinations in the handling of hip disease in young girls.

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PRIMARY HYDROCELE IN INFANCY.—All primary childhood hydroceles are congenital in origin and result from the distension of a patent processus vaginalis with peritoneal fluid. The ligation and division of a patent funicular process or strand is all that is necessary to cure the condition. Simultaneous evacuation of the hydrocele by aspiration or minute incision avoids waiting for the reabsorption of fluid which has been shown to follow the ablation of a patent processus. The more extensive interference with the hydrocele sac inherent in orthodox surgical procedures is therefore unnecessary. This interference, moreover, is sometimes followed by recurrence which is demonstrably due to a patent processus. Ligation and division of this processus will achieve a permanent cure.—Douglas G. McKay, R. Fowler, and J. S. Barnett, The Pathogenesis and Treatment of Primary Hydroceles in Infancy and Childhood, *The Australian and New Zealand Journal of Surgery*, August, 1958.

CARDIAC CATHETERIZATION IN CONGENITAL HEART DISEASE

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Experience with more than 2,000 cardiac catheterizations has been analyzed with respect to the merits of various techniques, the risks involved, and the value of the information gained. The technique described yields data on the pressure and oxygen content of the blood and on the intensity of the heart sounds at various points in the pulmonary artery system, the right ventricle, and the contributing systemic veins. The view that cardiac catheterization is dangerous should take into account the fact that these patients are examined in all stages of myocardial decompensation and many are in severe cardiorespiratory distress. In this series one death was attributed to the procedure. Because definitive treatment of congenital heart lesions is surgical, the information obtained by cardiac catheterization is needed in order to reduce the number of patients operated on for inoperable defects or denied operation for defects that could be corrected.

Catheterization of the right heart and pulmonary circuit has been used in the diagnosis and estimation of prognosis of congenital anomalies of the heart for several years. The present paper is based on the personal performance of over 2,000 studies. It will deal, briefly, with technique, risk, and value.

Technique

All of our young patients are asleep during the procedure. This offers three advantages: a steady state, avoidance of discomfort and apprehension, and speedy completion. Thiopental (Pentothal) sodium is used routinely, intravenously in older children and intramuscularly in infants.

Procaine hydrochloride is injected into the skin overlying the chosen vein. Choice of vein depends primarily on size of patient. In small infants the right saphenous vein is used; if this will not admit a catheter, the right femoral vein is substituted. In older infants the left brachial vein near the axilla is the route of choice; in children the left basilic vein in the antecubital space is preferred.

A small incision is made in the skin over the vein, and the vein and nearby artery (brachial or femoral) are isolated. Both vessels are secured for manipulation, the former by two loops of cotton suture, the latter by a rubber band.

The catheter is then introduced into the vein through a vertical incision and manipulated through the right side of the heart to the pulmonary circuit. In some patients the tip will pass to abnormal positions, e. g., the ascending aorta from the right ventricle via a ventricular septal defect; the left atrium, left ventricle, or pulmonary veins through an interatrial communication; or the descending aorta from the pulmonary artery through a patent ductus arteriosus.

When the catheter reaches the pulmonary artery it is advanced into the lung field as far as possible for determination of pulmonary venous capillary pressure. Then it is withdrawn in stages, always while pressure is being recorded, to various points in the pulmonary artery system, the right ventricle, and the right atrium and its contributory branches. At each point a blood sample, 2 to 3 cc., is secured for determination of oxygen content. As a rule these total 12. An arterial tracing and sample are obtained by direct cannulation of the artery. Theoretically, the samples from pulmonary and systemic arteries should be drawn simultaneously while oxygen consumption is being measured so that cardiac output can be calculated. In practice the measurement of oxygen consumption in the small patient is so inexact that calculated flows and shunts are relatively meaningless, and we do not bother with the determination.

In our laboratory oxygen content is measured by the Van Slyke apparatus. This is time-consuming and, in this respect, is inferior to direct oximetry. However, in our hands, oximeters have been undependable, whereas our Van Slyke technicians can always be trusted.

The actual catheterization procedure is usually completed within one-half hour, whatever the route used. The time during which the patient is exposed to fluoroscopy rarely exceeds four minutes, the average being three.

For several months we have been using intracardiac phonocardiography as a part of the procedure. After the steps detailed above, a second instrument is introduced into the vein and guided over the same route. This is a lumenless "catheter," at the tip of which is a tiny sound pick-up apparatus.[1] With proper amplifier, heart murmurs are heard and recorded at the point of origin and distally. For example, the murmur of a ventricular

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septal defect is heard in the distal portion of the right ventricle and in the pulmonary artery but not in the atrium; that of pulmonary stenosis, patent ductus arteriosus, or an aortic septal defect in the pulmonary artery but not in the ventricle; that of an atrial septal defect in the pulmonary artery (systolic) and in the right atrium (diastolic). This portion of the procedure necessitates about one minute of additional fluoroscopy time and adds 10 minutes to the over-all time of the study.

Risk

Right heart catheterization has been frequently represented as a dangerous study, to be avoided except for vaguely defined situations. Actually, when properly conducted, it is safer than many other procedures which are freely used.

This series includes patients in all stages of myocardial decompensation, in all age groups, and of all sizes. In the last 1,000 patients 284 were under one year of age. The youngest was less than 24 hours old; the smallest weighed 1,134 Gm. (2.5 lb.). There has been one death which may be attributed to the procedure. In this patient it could not be determined from clinical, radiologic, and electrocardiographic evidence if he had downward displacement of the tricuspid valve (Ebstein's disease) or pulmonary stenosis. He was in severe, intractable failure. Cardiac arrest occurred as the catheter was being withdrawn from the heart. At autopsy he was shown to have downward displacement of the tricuspid valve.

Five additional patients possibly would not have died at the time they did had catheterization not been scheduled. However, their deaths were not due to the catheterization. Three patients died before or during the cut-down. Another died while the vein was being isolated. All were in severe cardiorespiratory distress and might have died at any time. The last patient died approximately 24 hours after a catheterization which had been uneventful. He failed to awaken during the period before death. It is possible that in all the anesthesia was responsible.

Except for these deaths there have been no distressing complications. All types of arrhythmia may be induced by the stimulus of the catheter tip in certain areas; these have been transient and only rarely have prevented completion of the procedure.

Complications which have occurred in other laboratories include knotting of the catheter within the cardiovascular system, perforation of a vessel or chamber, embolus, or introduction of bacteria. These result, for the most part, from improper technique and should not be considered as inherent dangers.

The low mortality in this group is not exceeded in the experience of many others. To a growing number of pediatric cardiologists right heart catheterization is a part of the routine study of patients with evidence of significant congenital heart disease. The view that the procedure is dangerous and should be used rarely is difficult to comprehend in this day when open-heart surgery for congenital heart disease is so widely accepted. If a surgical technique which involves a relatively large mortality—and open-heart surgery does—can be accepted with equanimity, surely a safe diagnostic procedure should not be maligned.

Value

The proper treatment of a patient with congenital heart disease depends on exact anatomic diagnosis and proper assessment of the dynamic significance of the lesion. In general, heart defects affect the circulation in one or a combination of three ways: by interfering with blood flow to or from a chamber or vessel, by increasing flow to a chamber or vessel, or by decreasing flow to the myocardium. Because there is no uniformity in severity of defect, any one or any combination will produce a wide range of alteration in dynamics. Also, because there is no uniformity in quality of myocardium, there will be a wide range of response in patients to a certain defect of certain size or severity.

It is obvious, if one keeps in mind the course and determinants of the normal circulation, that defects of different anatomic location but of the same dynamic type will result in similar clinical signs and symptoms. They may result, too, in similar x-ray and electrocardiographic findings, because these, also, reflect dynamics and the individual's response to an added burden. Although there are combinations of such clinical data which point to a particular lesion in the majority, there is a minority in whom the same data are the result of an entirely different anatomic situation.

One experienced in the field of congenital cardiac disease will be correct in the clinical diagnosis in 80 to 90% of patients. He makes use of the history, physical signs, roentgenographic appearance, and electrocardiogram and adds the immeasurable advantage of experience and the hunch. If he is correct in 80 to 90%, it follows that in 10 to 20% his diagnosis is in error. Because definitive treatment of congenital heart lesions is surgical, this means that some of the 10 or 20 patients in each 100 are operated on in the face of an inoperable defect or are denied surgery although the defect could be corrected.

The routine use of cardiac catheterization in infants and children with evidence of significant congenital heart disease allows correct diagnosis in all but a small percentage of patients. This small number can be reduced further by use of contrast roentgenographic studies—angiocardiography and thoracic aortography.

It is in the infant age group that catheterization is particularly important and should be more frequently used. First, correct anatomic diagnosis based on the history, physical examination, x-rays, and the electrocardiogram is much more difficult in the very young infant than in the child, and we allow many to die needlessly because of failure to determine their true state. Second, the older child with congenital heart disease has, by surviving for several months or some years, demonstrated that he has the capacity to compensate for his defect. The infant may or may not prove to have this capacity. If he does not, and trouble suddenly occurs, his salvation may depend on the prior establishment of the exact nature of his defect.

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ANGIOCARDIOGRAPHY IN DIAGNOSIS OF CONGENITAL HEART DISEASE IN INFANCY AND CHILDHOOD

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Congenital anomalies of the heart exist in great variety, and no single diagnostic procedure suffices for differential diagnosis among them. Angiocardiography depends on making a rapid serial roentgenographic study of the heart and great vessels after a timed intravenous injection of radiopaque contrast substance. Its results in various types of malformation are described. It is not necessary in every case, and it is not always sufficient to settle the diagnosis. The patients who undergo angiocardiography have serious circulatory handicaps, yet there has been only one fatality during the procedure in more than 1,500 infants and children. When it offers the prospect of clarifying a diagnosis and deciding whether a case is operable, the risk involved in angiocardiography is less than the risks of not treating or incorrectly treating congenital heart disease.

Angiocardiography is the intravenous method, described by Robb and Steinberg,[1] of visualizing the cardiovascular structures. It is accomplished by the rapid injection (one and one-half seconds or less) of a concentrated organic iodide solution into an arm vein and making roentgenographic exposures of the cardiovascular system. Speed of injection is essential and is achieved by the use of a special 12-gauge needle–stopcock unit and a special 50-cc. Luer's syringe with a 12-gauge tip and by injection of the contrast substance during inspiration with the patient's arm elevated.[2] Sodium acetrizoate (Urokon sodium), 70%, has been found to be the contrast medium of choice, giving few side-effects and reactions. The dose of sodium acetrizoate for infants and children is 1 cc. per kilogram of body weight.

The new 12-by-12-in. roll film (F-X-R) magazine[3] will provide multiple (three per second) roentgenograms during opacification of the cardiovascular system. Serial studies in two planes, as many as 6 to 12 per second, and selective angiocardiography, secured by injection of contrast material through a catheter advanced into the heart, are further refinements in the diagnosis of congenital heart disease. However, the risks of selective angiocardiography, since it involves both cardiac catheterization and angiocardiography, are probably greater than those of the intravenous method. In special cases, as in aorticopulmonary shunt, aortography may be indicated.

Traditionally, congenital heart disease has been divided into the cyanotic and acyanotic types. Such a classification has served admirably to enhance diagnosis and treatment. However, alterations in physiological states may produce cyanosis in patients with conditions that ordinarily do not give rise to cyanosis (pulmonary stenosis, patent ductus arteriosus, atrial septal defect, and Eisenmenger complex). Inasmuch as angiocardiography is primarily an anatomic discipline, it seems worthwhile to classify congenital heart disease along such lines.

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Accordingly, congenital cardiac lesions have been grouped depending on whether there is (1) stenosis of a valve or vessel, (2) cardiac and great vessel shunts, (3) complex malformations (tetralogy of Fallot and transposition of great vessels), or (4) great vessel anomalies (pulmonary arterial, aortic, and pulmonary venous).

Stenosis of a Valve or Vessel

Pulmonary Stenosis.—There are two main types of pulmonary stenosis, valvular and infundibular. The valvular (fig. 1) consists of a dome-shaped membranous structure (opened umbrella-like) formed by the fused pulmonary cusps. An orifice, usually centrally located, can be identified by a "jet" of opacified blood. The valve cusps are mobile despite fusion and are easily recognized, especially during diastole. The right ventricle is enlarged, and during diastole thickening and trabeculation of the wall can be seen. The outflow tract of the right ventricle is of good caliber during diastole but may appear contracted and simulate infundibular stenosis during systole. Multiple stenosis of the pulmonary arteries, chiefly the main branches, has recently been reported and called coarctation of the pulmonary arteries.[4] Infundibular stenosis of the pulmonary artery rarely occurs as an isolated lesion. Usually it is associated with deformities of the ventricular septum, occurring in patients with tetralogy of Fallot and transposition syndromes.

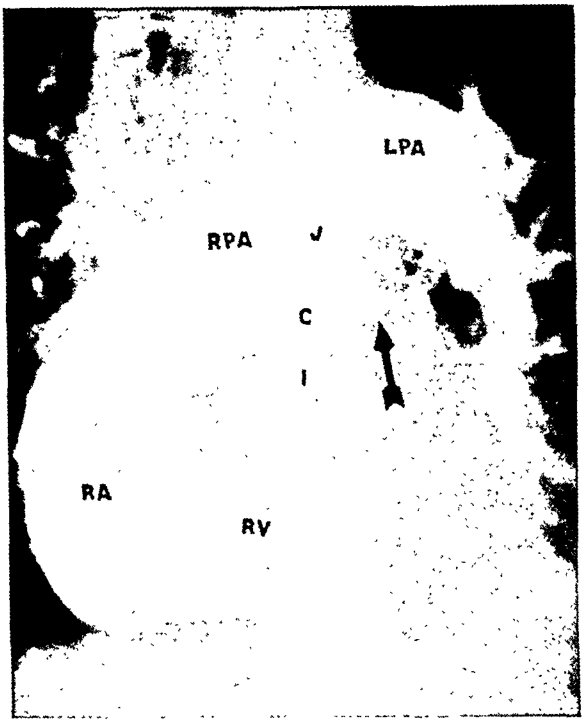

Fig. 1.—Pulmonary valvular stenosis in 7-year-old child. Frontal angiocardiogram reveals enlargement of right atrium (*RA*) and ventricle (*RV*). Infundibulum (*I*) of right ventricle ends in everted pulmonary cusps (*C*). Adjacent is dilated sinus of Valsalva of pulmonary artery (*arrow*). "Jet" (*J*) can be seen through the stenotic pulmonic valve, causing poststenotic dilatation of left pulmonary artery (*LPA*). In contrast is normal-sized right pulmonary artery (*RPA*). Note enlargement of central pulmonary arterial tree but decreased blood flow through lungs.

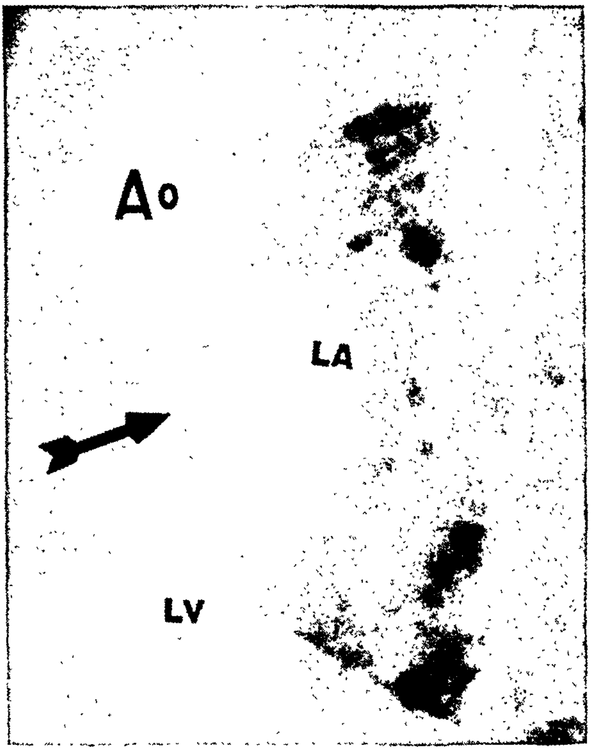

Fig. 2.—Angiocardiogram of 7-year-old child with history of aortic murmur since birth. Note deformed aortic cusps (*arrow*) and poststenotic dilatation of ascending aorta (*AO*). *LA*, left atrium; *LV*, left ventricle.

Aortic Stenosis.—Aortic stenosis may be divided into the valvular and subvalvular types. In the valvular type, the cusps are thickened and may be fused to form a dome-shaped diaphragm with a central opening. Frequently, there is poststenotic dilatation of the ascending aorta. Clinically, it is almost impossible to distinguish between aortic valvular and subaortic types of stenosis. This is also true after angiocardiography. Figure 2 shows dome-shaped deformities of the aortic cusps with poststenotic dilatation of the ascending aorta.

Congenital Mitral Stenosis.—Isolated congenital mitral stenosis is rare, but association with aortic valve, aorta, and ductus arteriosus malformations is not uncommon.[5] In the angiocardiogram, isolated enlargement of the left atrium, delay in emptying, and enlargement of the right ventricle and pulmonary artery is seen in uncomplicated congenital mitral stenosis (fig. 3).

Coarctation of the Aorta.—Angiocardiography in patients with coarctation of the aorta is customarily performed in the left anterior oblique projection; this affords an open view of the aortic arch similar to exposure during an operation. The angiocardiographic findings may be summarized as follows: The left ventricle may be enlarged. The ascending aorta, often normal in the young patients, is usually dilated in the adult. The innominate and left subclavian arteries are often dilated, and the left common carotid artery is frequently enlarged. Collateral channels, particularly the internal mammary and shoulder girdle arteries, may be dilated and tortuous. The intercostal arteries are not as well visualized. The exact site of coarctation is readily identified at a variable distance beyond the left subclavian artery (fig. 4). There is seen to be an area of abrupt constriction which is obscured in part by overlapping of the poststenotic segment of the aorta. The diameter of the lumen at the site of coarctation cannot be determined. Prompt filling of the aorta distal to the stenosis may occur via collaterals in the absence of any opening. The length of the stub of aorta distal to the left subclavian artery and proximal to the site of stricture has varied. Dilated intercostal arteries may occasionally be seen connecting with the poststenotic descending aorta. Rarely, an aneurysm of the intercostal vessels can be recognized.

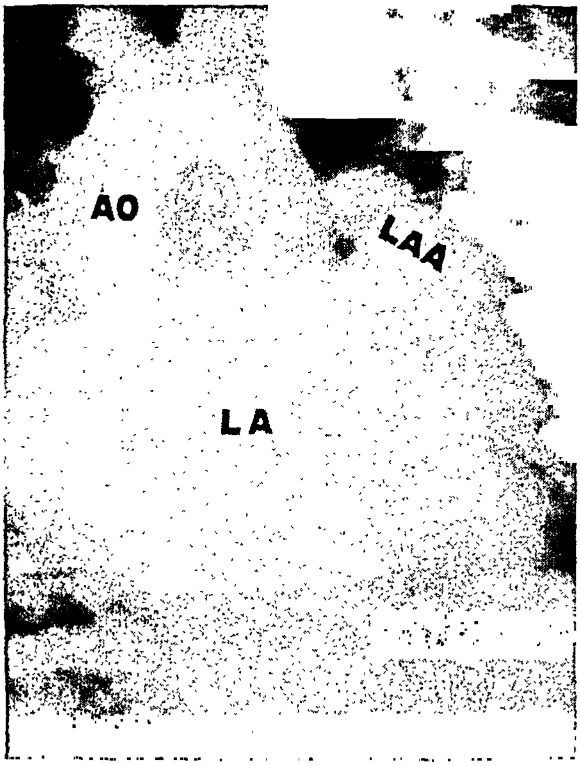

Fig. 3.—Congenital mitral stenosis in 21-month-old boy. Frontal angiocardiogram shows a markedly enlarged left atrium (*LA*). *LAA*, left atrial appendage; *AO*, aorta.

Simple Shunts

Atrial Septal Defects.—The angiocardiogram in atrial septal defect reveals right-sided heart and pulmonary arterial enlargement. The contrast agent can sometimes be seen to pass from the right to the left atrium. Filling defects due to left-to-right shunting of blood may be often recognized in the right atrium (fig. 5). Associated defects, such as pulmonary stenosis, tricuspid atresia, and anomalous drainage of pulmonary veins, frequently are accompanied by right-to-left atrial shunts. The usual finding is persistent opacification of the right atrium, right ventricle, and pulmonary arteries which lasts during the entire period of cardiac filling and results from recirculation of opacified blood from the left to the right atrium. Opacification of the chambers of the left side of the heart and the aorta is usually of poor quality due to dilution of the contrast agent by large volumes of shunted blood. Persistent opacification of the pulmonary arteries also occurs as a result of a large ventricular septal defect, patent ductus arteriosus, and defects in the aorticopulmonary septum, but the right atrium does not share in the opacification. It is occasionally difficult to establish with certainty that recirculation of contrast agent is actually present. A slow injection or the trapping of the contrast agent in arm or neck veins may result in prolonged filling of the right atrium and lead to a mistaken angiocardiographic diagnosis of an atrial defect.

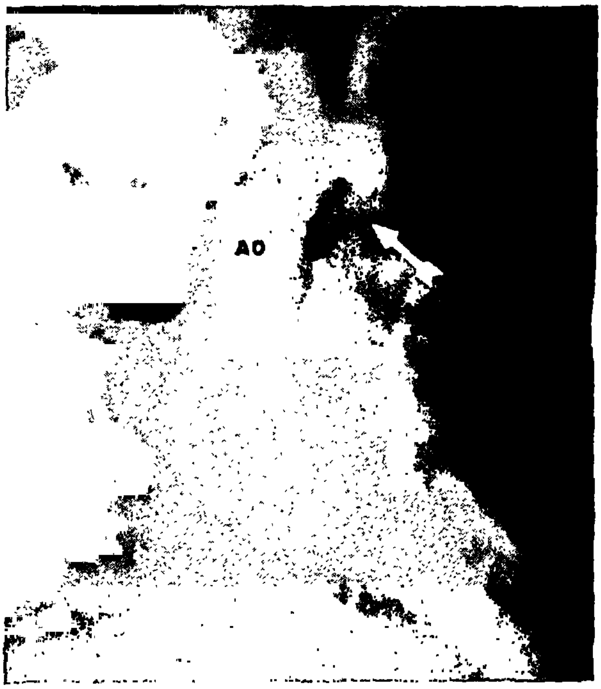

Fig. 4.—Frontal angiocardiogram, showing classic coarctation of aorta (*arrow*) in 6-year-old boy. *AO*, moderately dilated ascending aorta.

Ventricular Septal Defects.—Angiocardiography may show no abnormality in the presence of small defects in the ventricular septum. There may be evidence of reopacification of the right ventricle (but not the right atrium) at the time of left heart filling, but, as is the case with atrial defects, the finding is difficult to evaluate. In high ventricular septal defects there may be angiocardiographic demonstration of shunting of blood in both directions across the defect, especially with pulmonary hypertension (fig. 6). Even after cardiac catheterization it may be difficult to distinguish between such a lesion and the Eisenmenger complex.

Patent Ductus Arteriosus.—The angiocardiographic findings which have been observed in patients with patent ductus arteriosus include (1) dilatation of pulmonary arteries, (2) high position of the left pulmonary artery, (3) a defect in the column of contrast substance within and at the time of filling of the pulmonary artery and the left pulmonary artery caused by a "jet" of nonopacified blood issuing from the ductus (fig. 7*A*), (4) persistent opacification of the pulmonary arteries at the time of aortic filling (fig. 7*B*), (5) localized dilatation of the aorta at the site of origin of the ductus, and (6) rarely, opacification of the ductus itself. These signs have all been absent in patients with proved cases of patent ductus arteriosus. In some patients with patent ductus arteriosus the pulmonary arterial blood pressure may be elevated to systemic levels. When this occurs the direction of flow across the ductus becomes reversed with the production of typical clinical and angiocardiographic findings. As illustrated in figure 7*C*, early opacification of the descending but not the ascending aorta occurs. Later films show opacification of the ascending aorta and this rules out the presence of stenosis of the aortic arch. As would be expected, this situation results in cyanosis localized to the lower but not the upper extremities.[6]

Aortic Septal Defect.—Since the two lesions of patent ductus arteriosus and aorticoseptal defect produce the same hemodynamic abnormality, it is usually not possible by means of angiocardiography or cardiac catheterization to distinguish between patent ductus arteriosus and defects occurring between the aorta and the pulmonary artery just above the semilunar valves. Fortunately, the latter lesion is rare. The diagnosis may be suspected clinically and confirmed by thoracic aortography. Such defects have been occasionally repaired.

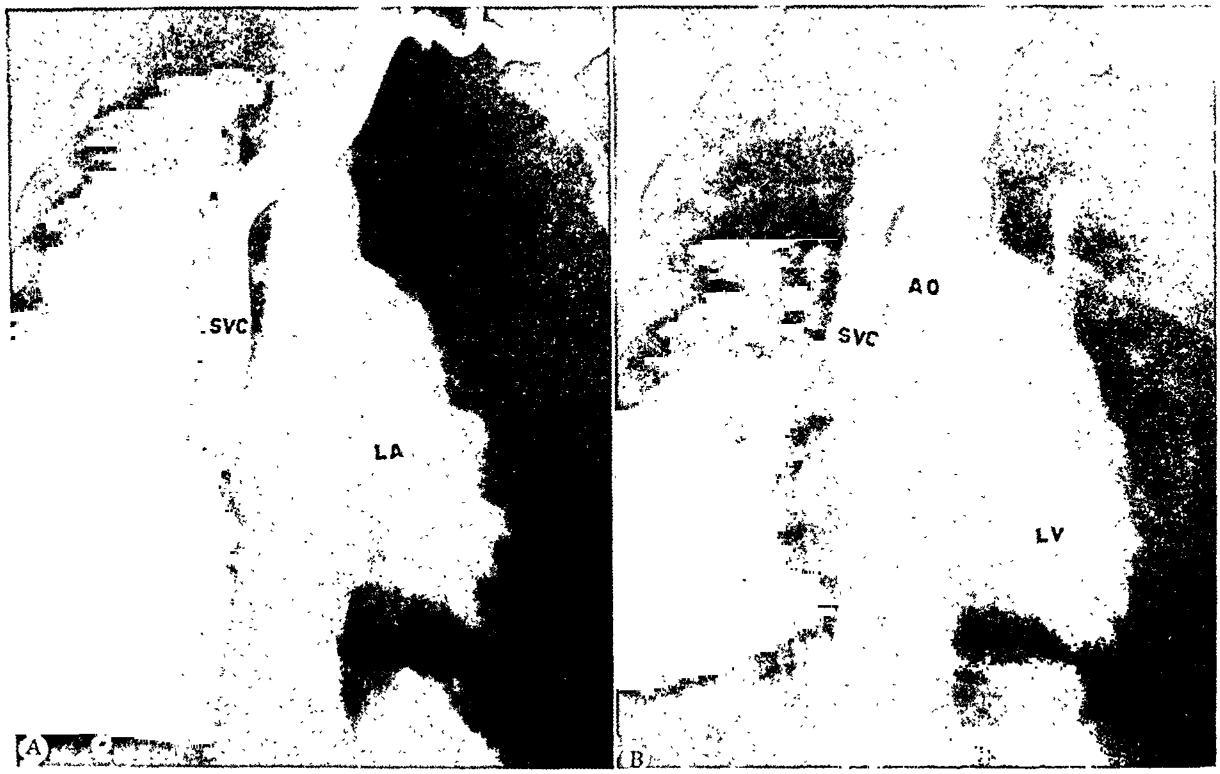

Fig. 5.—Huge atrial septal defect in 13-year-old girl. *A*, frontal angiocardiogram at one and one-half seconds shows the superior vena cava (*SVC*) emptying into left atrium (*LA*). Right atrium is nonopacified because of left-to-right flow through atria. *B*, a second later, left ventricle (*LV*) and aorta (*AO*) are opacified. *SVC*, superior vena cava.

Complex Malformations

Tetralogy of Fallot.—Tetralogy of Fallot consists essentially of the combination of two lesions, pulmonary stenosis (infundibular or valvular) and dextroposition or overriding of the aorta. A physiological if not an anatomic ventricular septal defect always occurs when the aorta overrides the ventricular septum, and right ventricular hypertrophy is the result of pulmonary stenosis rather than a fundamental component of the anomaly.

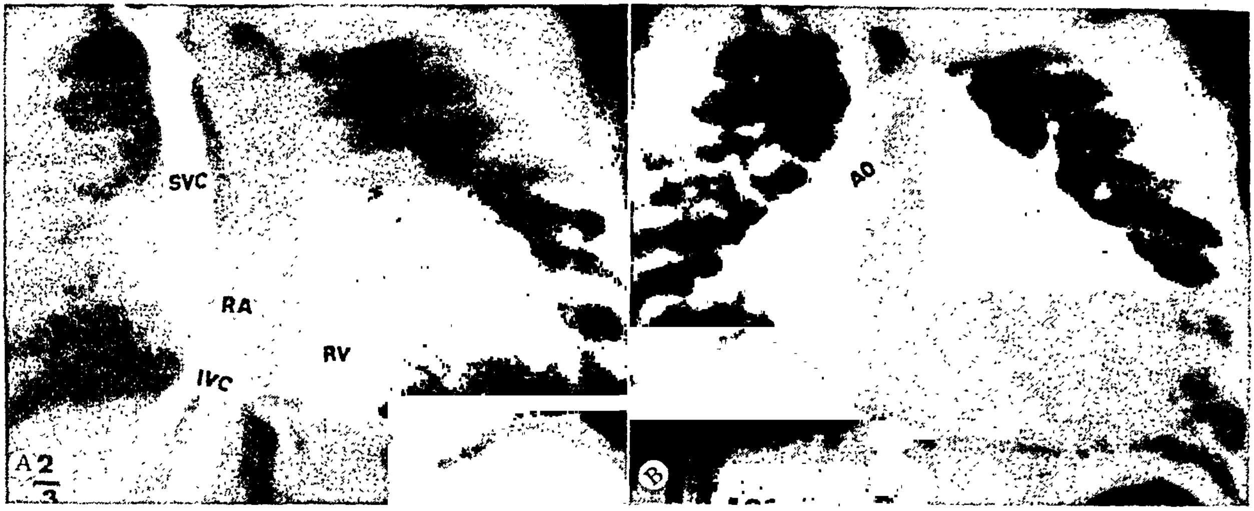

Fig. 6.—Ventricular septal defect in 3½-month-old infant. *A,* two-thirds second after injection, superior vena cava (*SVC*), right atrium (*RA*), inferior vena cava (*IVC*), and right ventricle (*RV*) are opacified. *B,* one second later, there is filling of plethoric lung vasculature and aorta (*AO*). At autopsy, a few days later, huge ventricular septal defect and pulmonary arteriolar sclerosis were found.

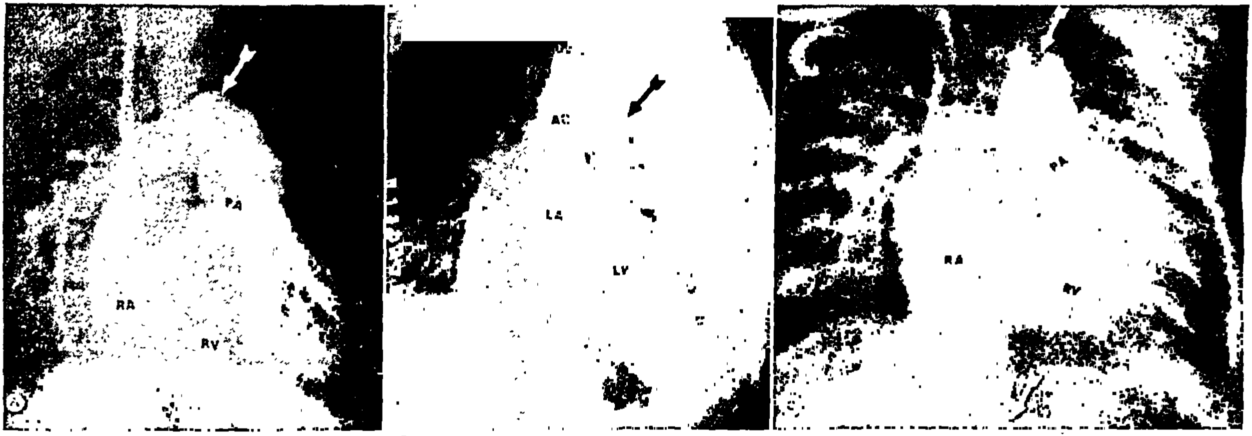

Fig. 7.—Patent ductus arteriosus exhibiting, *A* and *B,* "jet sign" in left pulmonary artery. *A,* frontal angiocardiogram of 14-year-old girl reveals rounded pinpoint area of nonopacification in left pulmonary artery (*arrow*). *PA,* pulmonary artery; *RV,* right ventricle; and *RA,* right atrium. *B,* when structures of left side of heart are filled (*LA,* left atrium; *LV,* left ventricle; and *AO,* aorta), there is reopacification of left pulmonary artery (*arrow*). *C,* reversal of shunt. Enlarged frontal angiocardiogram of 4-month-old infant shows filling of ductus arteriosus (*upper arrow*) and descending aorta (*lower arrow*) at time of filling of right side of heart (*RA,* right atrium; *RV,* right ventricle; and *PA,* pulmonary artery).

The angiocardiographic identification of pulmonary stenosis may be direct or indirect. Selective angiocardiography has considerably increased the yield of direct diagnosis of pulmonary stenosis.[7] In only about half the cases the pulmonary infundibular or valvular narrowing is seen with the intravenous method. The presence of stenosis may, however, be inferred with reasonable assurance from one or more of the following findings: 1. The peripheral pulmonary arteries are unusually small. 2. They fill poorly with opaque substance. 3. The central pulmonary arteries, even though fairly large and well filled, are irregularly deformed in appearance, while the peripheral branches are disproportionately small. Even though good filling of apparently normal pulmonary arteries is seen, pulmonary stenosis cannot be excluded by angiocardiography (although in such cases it is reasonable to conclude that marked reduction in pulmonary blood flow is not present). Furthermore, failure of the pulmonary arteries to fill with contrast substance may be the result of transposition of the great blood vessels rather than pulmonary stenosis.

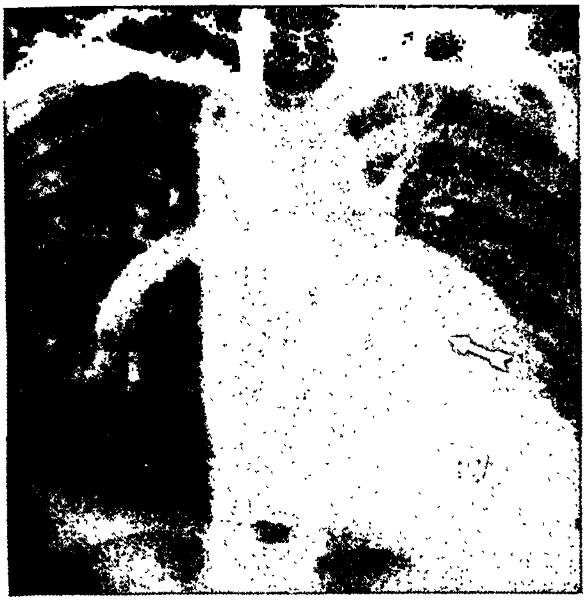

Fig. 8.—Angiocardiogram, at one and one-half seconds, showing tetralogy of Fallot in 4-year-old child, with simultaneous filling of huge right ventricle (*RV*) and dilated dextroposed aorta (*AO*). Arrow points to stenosis of pulmonary conus. Note decreased blood flow in lungs.

Dextroposition or overriding of the aorta is manifest in the angiocardiogram by the immediate passage of contrast agent from the right ventricle to that vessel, a direct angiocardiographic demonstration of the cause of the patient's cyanosis (fig. 8). In general, the degree to which the aorta overrides can be estimated from two findings. If early aortic opacification is faint as compared to the density in the pulmonary artery and as compared to that obtained later in the angiocardiographic series when contrast substance reaches the aorta from the left ventricle, it may be assumed that only slight dextroposition exists. Furthermore, the position of the base of the aorta with respect to the heart border and the contour of the aortic arch are of significance. The farther anterior the origin of the aorta and the more rounded-out its course throughout the thorax, the greater is the degree of aortic overriding. The so-called pseudotruncus arteriosus is a variant of the tetralogy of Fallot in which the pulmonary artery is markedly stenotic if not atretic, circulation to the lungs being via bronchial arteries.

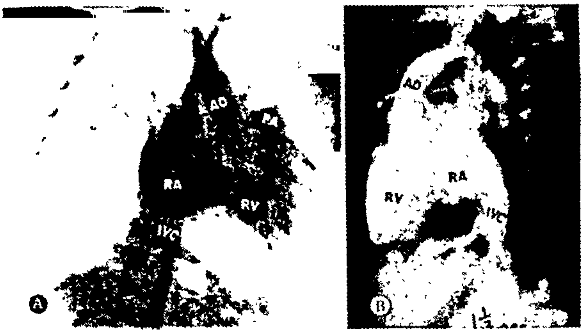

Fig. 9.—Transposed great vessels in 5-month-old infant. *A*, frontal angiocardiogram at two and one-third seconds shows a dextroposed aorta (*AO*) arising from right ventricle (*RV*). Enlarged right atrium (*RA*) and inferior vena cava (*IVC*) are also opacified. Pulmonary artery (*PA*) is just beginning to fill. *B*, lateral angiocardiogram at one and one-third seconds demonstrates anterior position of aorta (*AO*) arising from right ventricle (*RV*). *IVC*, is inferior vena cava; right atrium (*RA*) is also opacified.

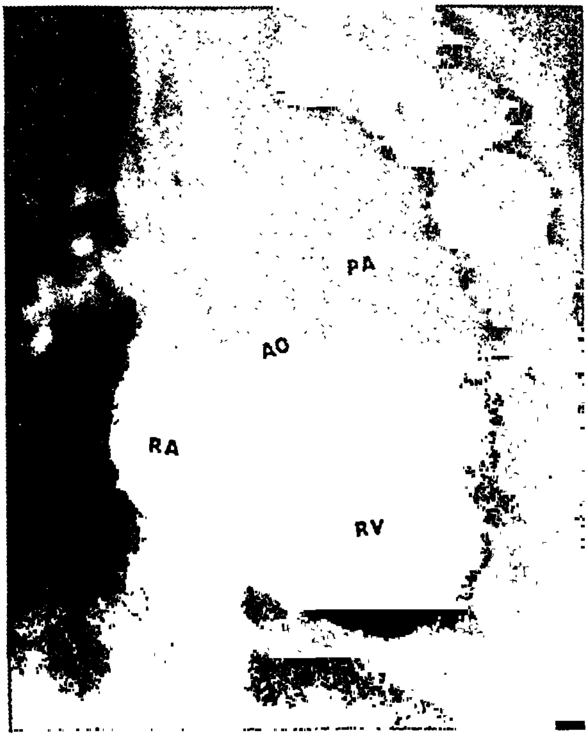

Fig. 10.—Taussig-Bing syndrome in 5-year-old child. Frontal angiocardiogram at one and one-half seconds shows simultaneous filling of huge pulmonary artery (*PA*) and dextrorotated aorta (*AO*). *RV*, common right ventricle; *RA*, right atrium; *arrow*, descending aorta.

In summary, the angiocardiographic diagnosis of tetralogy of Fallot depends on the simultaneous filling of the aorta and pulmonary artery from the right ventricle and the demonstration of pulmonary stenosis. Infundibular stenosis of the right ventricle is probably the commonest type of pulmonary deformity although the valvular or the combination of both types may occur. In most cases the main pulmonary artery is diminished in caliber, but in others it is of normal size. In severe degrees of pulmonary stenosis the pulmonary artery is apt to be small and fills later than the opacified aorta. Poststenotic dilatation of the pulmonary artery occurs more frequently in valvular than in infundibular stenosis. The pulmonary vasculature can often best be evaluated by angiocardiography. In the tetralogy of Fallot it is strikingly diminished.

Angiocardiography readily demonstrates associated anomalies of the aortic arch and branches. A right aortic arch and the position of the branches may be often a determining factor in the type of aorticopulmonary operation; i. e., whether Potts's anastomosis or the Blalock-Taussig operation is done.

Eisenmenger Complex.—In the Eisenmenger complex there is an overriding aorta associated with pulmonary hypertension. Angiocardiographically, the overriding aorta and pulmonary artery are often filled simultaneously from the right ventricle. However, with a slight degree of overriding the aorta may be only faintly filled. The differential diagnosis between the Eisenmenger complex and a high ventricular septal defect is made with great difficulty even after cardiac catheterization. Marked enlargement of the main stem pulmonary artery and dilatation of the pulmonary and peripheral branches with dense opacification are usually present.

Transposition of the Great Blood Vessels.—It may be difficult to distinguish with certainty between extreme dextroposition of the aorta associated with severe pulmonary stenosis and complete transposition of the aorta and pulmonary artery, particularly when pulmonary stenosis complicates transposition. The aorta in transposition "takes off" far anteriorly and describes an open, rounded course through the upper part of the thorax (fig. 9). The density of contrast substance within the aorta closely approximates that within the right ventricle. If the pulmonary arteries appear prominent in the conventional roentgenogram or unusually pulsatile at fluoroscopy and yet fill poorly or not at all during angiocardiography, transposition of the aorta and pulmonary artery should be strongly suspected. When pulmonary stenosis is present, the diagnosis may be even more difficult. Although in patients with transposition of the great blood vessels life is dependent on some intercommunication between the systemic and pulmonary circuits, these shunts are rarely demonstrated by angiocardiography.

Taussig-Bing Syndrome.—In the Taussig-Bing syndrome a transposed aorta and a large pulmonary artery arise from the right ventricle primarily; the pulmonary artery partially overrides the ventricular septum. A high ventricular septal defect and right ventricular hypertrophy complete the syndrome. The diagnostic angiocardiographic feature consists of simultaneous filling of the dilated pulmonary artery and aorta, differentiating it from the ordinary transposition. However, this is not pathognomonic, since transposition with a large ventricular septal defect can produce the same picture. Outlining

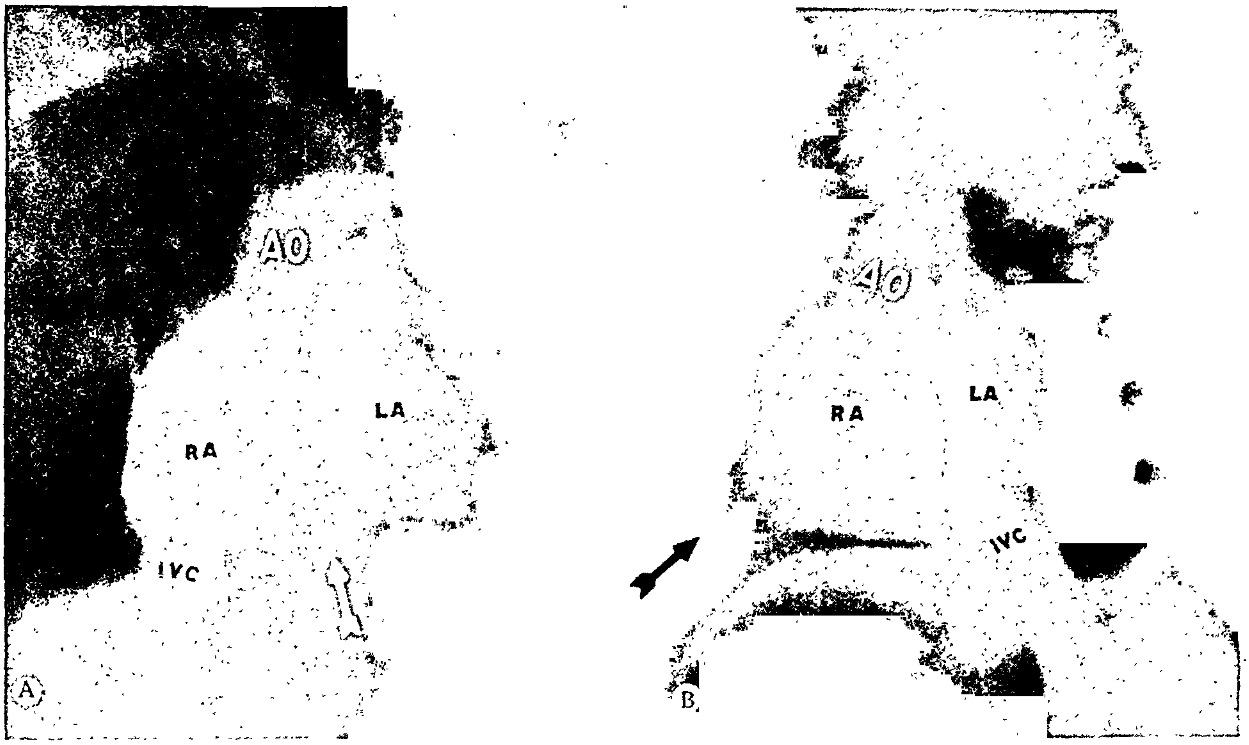

Fig. 11.—Tricuspid atresia in 4-month-old infant. *A,* angiocardiogram reveals enlarged right atrium (*RA*) being opacified from the inferior vena cava (*IVC*). Right ventricle (*arrow*) is unopacified, while left atrium (*LA*) is filled via atrial shunt. Ascending aorta (*AO*) is also opacified. *B,* lateral angiocardiogram shows unfilled right ventricle (*arrow*). Right atrium (*RA*) and left atrium (*LA*) are opacified via septal defect. *IVC* is inferior vena cava; aorta (*AO*) is also opacified.

the ventricular septum with a clear origin of the pulmonary artery from both ventricles and transposition of the aorta are essential for diagnosis of this complex (fig. 10).

Tricuspid Atresia.—In tricuspid atresia blood flow is from the right atrium across an atrial defect into the left ventricle and then into the aorta and pulmonary arteries. The origin of the great vessels may vary considerably. Both may arise from the left ventricle; either may arise from a diminutive right ventricle which receives blood from the left ventricle via a ventricular septal defect. Pulmonary stenosis may occur as may an associated patent ductus arteriosus. As is illustrated in figure 11, angiocardiography usually reveals the abnormal course of blood flow clearly. In this example the aorta takes origin from a diminutive, nonfunctioning right ventricle (filled via an interventricular septal defect) while the small pulmonary arteries give evidence of pulmonary stenosis. In another case reported elsewhere [8] tricuspid atresia was associated with dextrocardia, a common atrium, an anomalous pulmonary vein entering a left superior vena cava, a functioning single ("left") ventricle, severe pulmonary stenosis, and a large patent ductus through which blood reached the lungs. All the anatomic features except the tricuspid atresia itself were clearly shown in the angiocardiogram. Since the presence of tricuspid stenosis or atresia may be considered highly probable when cyanosis and left axis deviation of the electrocardiogram occur together, angiocardiography need be used only when operation is contemplated or in atypical cases.

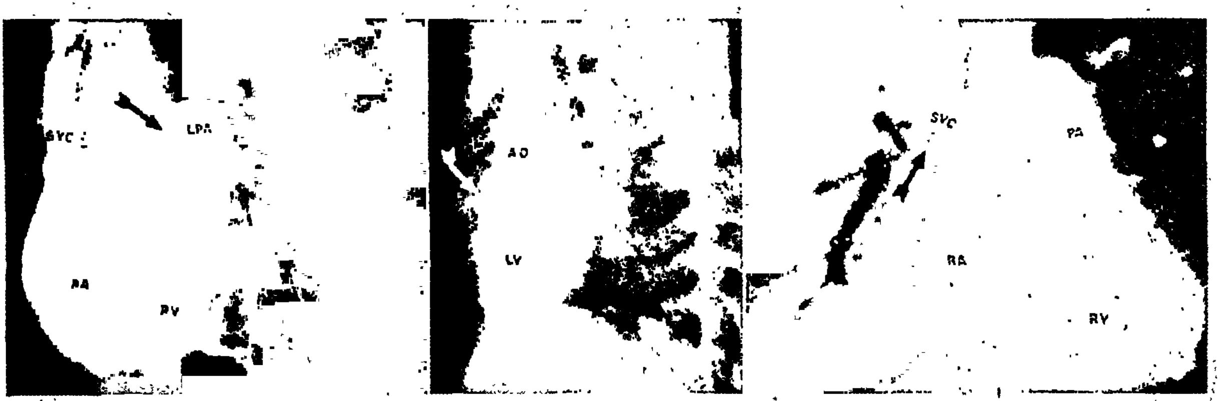

Fig. 12.—Anomalies of large arterial vessels. *A*, congenital absence of right pulmonary artery in 12-year-old girl. Frontal angiocardiogram at two and one-half seconds shows filling of right heart structures (*SVC*, superior vena cava; *RA*, right atrium; *RV*, right ventricle; and *LPA*, left pulmonary artery; and, *arrow*, absent pulmonary artery). *B*, Marfan's syndrome in 2-year-old twin with aneurysmal dilatation of aortic sinuses (*arrow*). *LV*, left ventricle; *AO*, ascending aorta. *C*, frontal angiocardiogram in 14-year-old girl, showing insertion of anomalous pulmonary veins at junction of superior vena cava (*SVC*) and right atrium (*RA*). Right ventricle (*RV*) and pulmonary artery (*PA*) are opacified. *Arrow*, "jet" made by unopacified blood from pulmonary veins joining opacified cardiovascular structures.

Anomalies of the Large Arterial Vessels

Pulmonary Artery.—Idiopathic or primary dilatation (aneurysm) of the pulmonary artery is rare. Angiocardiography readily demonstrates enlargement of the pulmonary artery. However, the diagnosis of primary dilatation of the pulmonary artery can be made only when the many causes of pulmonary artery dilatation, such as pulmonic stenosis, congenital heart disease (atrial and ventricular septal defects and patent ductus arteriosus), rheumatic heart disease, cor pulmonale, heart failure, and syphilis, are excluded. It rarely causes disability and requires no treatment.

Either a right or left main branch of the pulmonary artery may be congenitally absent, and the diagnosis of this newly recognized entity can often be made by conventional roentgenography. There is displacement of the mediastinum (mediastinal herniation), trachea, and heart by an overdistended lung, while the opposite lung is hypoplastic and poorly vascularized. The angiocardiographic study demonstrates the absence of a pulmonary artery with good vascularity of the overdistended lung. Studies with use of rapid, serial roentgenograms have disclosed that the bronchial arterial circulation is responsible for the poorly vascularized lung. Experience in three cases indicates that absence of a main branch pulmonary artery, when uncomplicated, is usually discovered during routine chest x-ray survey. The condition may be mistaken for a mediastinal tumor. This anomaly, when uncomplicated, requires no treatment, and the prognosis is good. However, such patients must be kept under observation, for the occurrence of pneumonia in the normal lung may wreak havoc with the gaseous exchange processes. Absence of a main branch pulmonary artery may also occur in association with cyanotic congenital heart disease [9] (fig. 12*A*).

Aorta.—Aneurysms of the aortic sinuses (of Valsalva) are rare and may be congenital or acquired. The acquired types are chiefly due to syphilis or bacterial endocarditis. The congenital aneurysms are thought to be due to a developmental defect in either the aorticopulmonary septum or the elastic tissue of the aortic sinuses. Diagnosis during the patient's lifetime with the aneurysm in an unruptured state can be made by angiocardiography[10] (fig. 12*B*).

Pulmonary Veins.—In 1949, partial anomalous insertion of the right pulmonary vein into the inferior vena cava was first diagnosed during life by angiocardiography and cardiac catheterization. Since then, recognition of totally anomalous pulmonary drainage into the right atrium and its tributaries has also become possible. Diagnosis of these conditions is important; the reanastomosis of pulmonary veins into the proper atrium in specially selected cases may be lifesaving. On the other hand, patients with partial anomalous pulmonary venous drainage complicated by a large atrial septal defect, pulmonary stenosis, or acquired rheumatic heart disease with mitral stenosis may be seriously handicapped and require operation. Complete study with cardiac catheterization as well as angiocardiography is necessary for full evaluation. Similarly, thorough study is indicated in patients suspected of having totally anomalous pulmonary venous drainage.[11]

When anomalous pulmonary veins from the lungs or the whole left lung insert into the left innominate vein, a characteristic roentgenographic picture results. The abnormal mediastinal and hilar shadows have been likened to a "figure of eight," a "dumbbell silhouette," a "mediastinal mustache," and a "cottage loaf." On angiocardiography, the widened mediastinal and hilar shadows on the left are seen to be due to the dilated common pulmonary venous trunk (persistent left superior vena cava) inserting into the left innominate vein, while on the right side they are due to the dilated superior vena cava enlarged because of the increased blood flow from the left innominate vein.

Total insertion of pulmonary veins into the superior vena cava and right atrium was found in a patient along with an associated atrial septal defect. (In total anomalous pulmonary venous drainage this must exist for life.) The conventional chest roentgenogram suggested the diagnosis because of an anomalous pulmonary vessel at the right base. Angiocardiography (fig. 12*C*) confirmed the diagnosis by showing the newly recognized "jet sign," a filling defect at the site of insertion of the anomalous veins into the junction of the superior vena cava and right atrium, and the demonstration of the insertion of the anomalous veins. The filling defect is due to the turbulence created by the anomalous pulmonary venous blood flow.

Summary

Angiocardiography is not indicated in every case of congenital heart disease because the physical, electrocardiographic, and conventional roentgenographic examinations provide a high degree of accuracy in diagnosis of cardiovascular disease. Furthermore, the complex types of congenital heart disease may also be difficult to diagnose even after angiocardiography and cardiac catheterization. However, considerable diagnostic data are obtained by contrast cardiovascular studies.

Fatalities after angiocardiography have been reported chiefly in the group of cases of cyanotic congenital heart disease. However, despite double injections to provide frontal and lateral views, only one fatality, and that in a child with primary pulmonary hypertension, has occurred in a series of over 1,500 infants and children. Accordingly, because the mortality of congenital heart disease is unusually high, it would appear that the failure to recognize a type of heart disease amenable to surgical repair provides a greater risk than angiocardiography.

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USE OF THE STETHOSCOPE IN PEDIATRIC CARDIOLOGY

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The stethoscope, as contrasted with numerous diagnostic auxiliaries, remains the major instrument in pediatric cardiology. It is portable, immediately informative, and adaptable to countless special situations; its usefulness is not limited to auscultation of the chest. Following hemodynamic sounds either to their point of maximum intensity or to their disappearance often leads to the neck and head. In children the pliability of the thoracic wall makes auscultation especially informative because heart sounds in some cases appear and in other cases disappear during manipulation of the chest. The investigation of both functional and organic murmurs is thus facilitated. Four characteristic murmurs or cardiovascular noises not related to disease occur in children up to 12 or 15 years of age and are here described. The stethoscope is the only instrument sufficiently versatile to permit bedside investigation of these interesting and significant phenomena.

While diagnostic auxiliaries to the stethoscope have become increasingly complex and effective, this acoustic aid continues to be a major instrument in the practice of medicine and especially in pediatric cardiology. Heart sounds and murmurs are not always pathognomonic diagnostically. They can be amplified or recorded electronically, but the stethoscope remains the portable and indispensable tool of the physician. It is important that the instrument be adequate and equipped for both bell and diaphragm auscultation.

Identification of Functional Murmurs

In infancy and childhood the routine auscultation of the heart must be varied from this examination in the adult. The predominant murmurs are different, their radiations are not the same, and even new techniques of auscultation can be applied to young children.

Most infants and children up to 12 or even 15 years of age have cardiovascular noises, or murmurs, which are not related to the presence of disease. While the term may be debatable, it has been conventional to call these murmurs functional in origin and common usage has made this term acceptable and its meaning clearly understood. There are four characteristic functional murmurs in children.

First, murmur is frequently heard in infants while the anterior fontanelle is open; it is maximum over the fontanelle and rather continuous. It is not related to intracranial vascular disease unless there is other evidence for this. The murmur usually is not present during the first few months of life.

Second, after the fontanelles are closed, it is common to find a systolic bruit bilaterally over the head and especially over the mastoid area. If this is equal and symmetrical, it is a normal hemodynamic noise and does not represent a vascular anomaly.

Third, the most common and best known of the normal vascular hemodynamic noises is the continuous murmur maximum at the jugular bulb on the right—the venous hum mentioned in the pediatric literature. This is almost uniformly loudest in the right, anterior, midportion of the neck but occasionally is maximum on the left. The reason for its predominance on the right is that about two-thirds of the intracranial venous drainage is through the right internal jugular vein. Occasionally this murmur is loudest on the left when, presumably, the maximum flow is on the left.

This murmur is easily manipulated by pressure on the vein and by changes in position of the head. This murmur is transmitted downward with the venous inflow into the thorax and, when heard only by auscultation over the precordium alone, is considered as intracardiac in origin; but disappearance or marked diminution of the neck murmur on manipulation greatly affects the intensity of the precordial murmur, and the relationship is readily demonstrated by the stethoscope.

Most commonly, this characteristic functional murmur is maximum at the second left interspace. When it is of the usual variety, pressure on the jugular bulb, rotation of the head, or lifting of the head by the patient himself promptly diminishes the murmur. The latter maneuver apparently fixes the thorax and diminishes resonance as well, changing the jugular murmur. The murmur is more likely to be maximum in the third interspace in small infants, when it has a peculiar crescendo quality.

It is, therefore, necessary that routine auscultation be extended beyond the precordium and especially into the supraclavicular areas. Following hemodynamic sounds by auscultation either to their point of maximum intensity or to their disappearance frequently leads to the head, and inclusion of the head and neck in routine auscultation is often rewarding. It is necessary to know the normal hemodynamic sounds to identify abnormal sounds.

Fourth, there are other common murmurs in children which are more difficult to interpret. There is also a harder, more constant, less maneuverable systolic murmur in the neck. This is thought to be arterial in origin. Approximately the same murmur

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Read in the Symposium on Pediatric Cardiology before the Joint Meeting of the Section on Diseases of the Chest and the Section on General Practice at the 107th Annual Meeting of the American Medical Association, San Francisco, June 27, 1958.

may be heard from the first or second left interspace to or beyond the apex without appreciable change by manipulation and without any real point of maximum intensity.

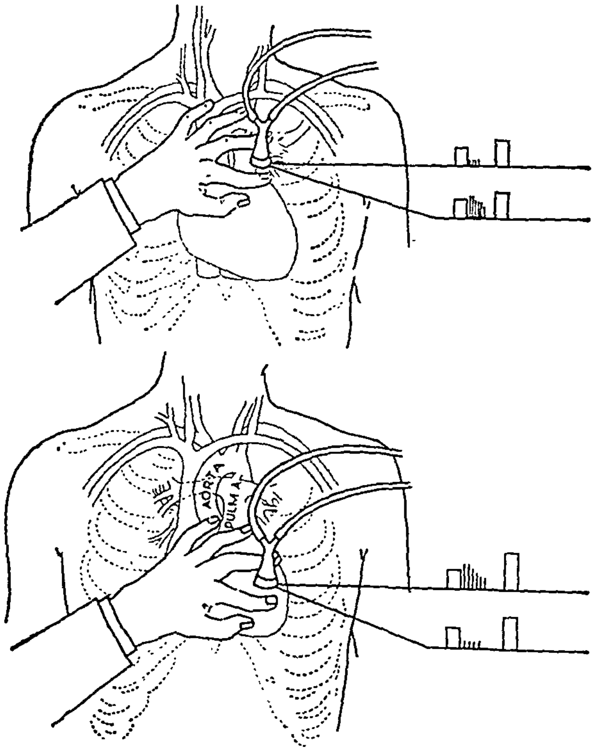

Fig. 1.—*Top,* accentuation of relatively faint systolic murmur in second left interspace by external pressure over this area. Bottom line indicates relative increase in intensity over usual murmur shown above. *Bottom,* diminution of systolic murmur at third left interspace. Artifacts resulting from pressure make phonocardiogram difficult to record in this position.

This is difficult to interpret, but most of these widespread, grade-2, systolic murmurs not associated with other evidence of heart disease will eventually localize at the second left interspace and be considered to be functional in nature. A few will localize at the apex and apparently represent mitral valve disease.

Organic Cardiac Disease

The stethoscope separates cardiac murmurs due to disease from the frequent, normal, hemodynamic noises. The murmurs and abnormal sounds related to heart disease are well known, and both the specific pathognomonic auscultatory findings and those which serve only as a basis for differential diagnosis are familiar. There are differences in the auscultatory manifestations of organic lesions in children and those of the same lesions in adults, and these differences are quite important to the cardiologist seeing both children and adults. An example are the murmurs related to disease of the aortic valve. In children both the diastolic murmur of aortic regurgitation and the systolic murmur of congenital aortic stenosis may be predominant at the left sternal border.

In general, the pediatric cardiologist is a specialist in diseases of the right side of the heart, and in congenital heart disease the left ventricle is less frequently affected. Of particular interest, therefore, is the identification of increased pulmonary artery flow or obstruction to flow by estimation of the pulmonary second sound. With observation and experience with the stethoscope the clinical diagnosis of the status of the pulmonary pressure may be approximated in terms of reduced, average, increased, or greatly increased. The necessity of remarking on the reduplication or splitting of this sound is obvious.

Manipulation of Murmurs

The labile cartilaginous thoracic cage of the infant and child can be sufficiently changed by extrinsic pressure so that the cardiovascular dynamics can be altered and, consequently, the resulting murmurs. Thus, murmurs due to organic disease can be changed as well as functional murmurs manipulated. While this area of manipulation of murmurs has not been fully explored, there are two bedside stethoscopic observations which are sometimes useful. Since the right ventricle lies immediately under the movable thorax, it is assumed that changes from anterior pressure on the thorax distort this most. Pressure should be applied firmly but cautiously until it is certain that minor arrythmias, especially premature systoles, are not induced. Rarely, short episodes of sinus arrest occur, and pressure should not be exerted without simultaneous auscultation. The arrythmias disappear at once on release of pressure.

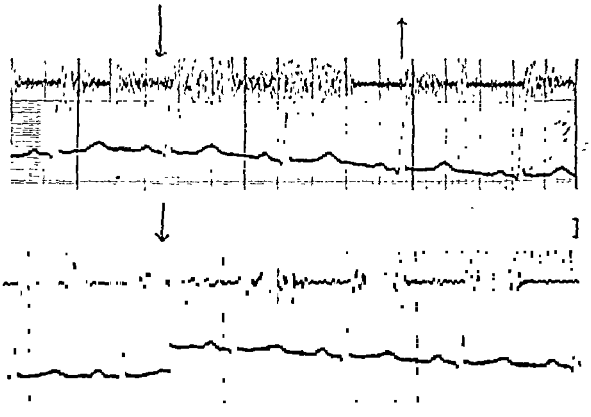

Fig. 2.—*Top,* phonocardiogram showing great increase in intensity of systolic murmur. Augmentation starts with external pressure and stops with release of pressure, as shown by arrows. *Bottom,* accentuation of murmur within one heartbeat of application of external pressure. Murmur is later in systole.

Short systolic murmurs maximum in the second left interspace which are too loud for the common functional murmur and not sufficiently loud for the diagnosis of pulmonary stenosis can be greatly accentuated by pressure at this area. Figure 1, *top,* demonstrates this augmentation schematically, and figure 2 shows phonocardiograms illustrating this.

Pressure is applied and released at the arrows. The spectacular increase in the intensity of the systolic murmur is obvious.

Patients who had had a complete cardiac examination, including cardiac catheterization, showed no abnormalities of right heart pressure and no abnormal flows could be discovered. It is believed that a minor defect of the pulmonary valve which was just sufficient to produce an audible systolic murmur was further distorted by extrinsic pressure and the murmur of mild pulmonary stenosis made obvious. This stethoscopic observation can be readily duplicated in certain patients. If the explanation is correct, the use of the stethoscope is extended.

Systolic murmurs sufficiently loud to be generally accepted as organic in origin may be sometimes measurably diminished and rarely obliterated by the same maneuver applied at the third or fourth interspace. These murmurs are similar to those usually thought to represent a small interventricular defect, and their disappearance is sometimes striking. Figure 1, *bottom,* illustrates this diminution schematically. In this position the phonocardiogram is difficult to record.

It is believed that the diminution or disappearance of organic murmurs indicates that the defect is small and easily partially occluded by anatomic distortion. The actual changes in hemodynamics have not been proved. But the bedside stethoscopic observation of murmur change by extrinsic manipulation can be easily duplicated in some patients, providing the thoracic wall is pliable. These observations are not applicable to adults.

Murmurs originating in the left ventricle cannot be manipulated. Likewise, it is believed that large shunts cannot be appreciably affected. But it is suggested that effort to manipulate the usual childhood functional murmur, the murmur of uncertain origin, and even the murmur of frank organic disease is always interesting and frequently rewarding.

920 E. 59th St. (37).

THE COURSE OF ACTIVE TUBERCULOSIS COMPLICATED BY PREGNANCY

Capt. Paul Flanagan
and
Major Nestor M. Hensler, (MC), U. S. A. F.

The course of tuberculosis was observed in a group of 22 pregnant women and compared with that in a group of 40 nonpregnant women of the same average age (23 years). The two groups were also similar in regard to the status of the disease. The progress of each patient was assessed in terms of rates of stabilization of the disease, of conversion of sputum and gastric washings, and of cavity closure. No significant difference between the two groups was discernible by any of these three criteria. There was no evidence that pregnancy affected the prognosis of tuberculosis provided the disease was treated the same in the pregnant as in the nonpregnant woman. The treatment consisted of certain combinations of isoniazid, streptomycin, and para-aminosalicylic acid. The obstetric results in the pregnant group were excellent; 21 had full-term, normal deliveries of healthy babies.

Active tuberculosis in pregnancy poses a frightening specter for the physician as well as the patient. The problem is not rare; in fact, in a recent series of 7,500 prenatal patients, 1% were found to have active disease.[1] The pre-chemotherapy literature on this subject presents conflicting opinions, and the literature of the chemotherapy era is scant. To help clarify the approach to the problem of handling the pregnant patient with active tuberculosis a retrospective analysis of our cases was undertaken.

Materials and Methods

The material for this study consisted of all patients admitted to the 2,349th U. S. A. F. Hospital between December, 1955, and December, 1957, in whom active pulmonary tuberculosis and pregnancy coexisted. These were compared with a control group consisting of all female patients in the same age range with active tuberculosis not complicated by pregnancy. There were 22 patients in the study group and 40 controls. All of the patients studied were hospitalized for at least six months, or until stability was achieved.

From the Pulmonary Disease Service, U. S. A. F. Hospital, Parks Air Force Base, California.

On admission, six sputum or gastric specimens were taken, concentrated, inoculated onto Löwenstein-Jensen medium, and allowed to incubate until growth was evident, or for nine weeks. Monthly specimens were studied thereafter. Monthly x-rays were taken. Lung cavities were confirmed or ruled out by appropriate planograms, Bucky films, and special views.

Background Data.—The two groups are remarkably similar as to age, the extent of disease on admission, presence or absence of cavity, and results of initial bacteriological studies (tables 1 and 2). Approximately 60% of the patients in each group had moderately or far-advanced tuberculosis with cavitation. Positive results of sputum or gastric bacteriological tests were obtained in 75% of the control group and 60% of the study group. Three patients in the control group and four in the pregnant group had received prior treatment for active tuberculosis, but only one in each group had received prior drug therapy; the rest were "original treatment" cases.

Drug sensitivity studies were obtained on initial cultures from 9 patients in the study group and 16 in the control group. Only one of these showed significant resistance to any of the three major antituberculous drugs. This patient, pregnant on admission, had received three years of streptomycin and aminosalicylic acid therapy elsewhere, and her organisms showed in vitro resistance to 100 mcg. per milliliter of these drugs.

TABLE 1.—*Background Data on Patients with Active Tuberculosis*

	Nonpregnant	Pregnant
Patients, No.	40	22
Born outside United States	10	8
Age		
15-19	6	5
20-24	19	11
25-29	15	6
Range	16 to 29 years	18 to 29 years
Mean	23	23
Median	23	23
Mode	23	23
S. D.	12	9

The dosage schedules varied (table 3). Thirty-one (77.5%) of the nonpregnant and 20 (91%) of the pregnant patients received isoniazid as part of their chemotherapeutic program. Two of the pregnant group as compared to nine of the nonpregnant group received only streptomycin and aminosalicylic acid. Otherwise the distribution of schedules was not greatly dissimilar.

Duration of symptoms prior to diagnosis and roentgenologic evidence of disease prior to hospitalization were comparable, and there were few complicating conditions. Three (13%) of the patients in the pregnant group were anemic, with hemoglobin concentrations of less than 10 Gm. per 100 cc., as compared to six (16%) in the nonpregnant group. Also, in the nonpregnant group there were two patients with active coccidioidomycosis as well as two with chronic alcoholism. In the control group there were six patients who had been pregnant within one year of onset of roentgenologically demonstrable changes or symptoms. *Evidence of disease developed more than two* months after delivery in all six cases.

TABLE 2.—*Status of Disease*

	Nonpregnant		Pregnant	
	No.	%	No.	%
Extent				
Minimal	16	40	9	41
Moderately advanced	16	40	9	41
Far advanced	8	20	4	18
Cavity present on admission	24	60	13	59
Positive bacteriological test at onset of treatment	30	75	14	64
Previous episode of tuberculosis	3		4	
Previous drug treatment for tuberculosis	1		1	
Pregnancy occurring after an episode of tuberculosis	0		4	
Pregnancy before this episode of tuberculosis	20	50	8	36
Duration of symptoms before hospitalization, mo.				
None	16		9	
Less than 1	8		5	
1 to 2	6		4	
2 to 6	7		2	
More than 6	3		2	
Duration of roentgenologic evidence of disease, mo.				
Less than 1	24		10	
1 to 2	11		9	
More than 2	5		3	

Results

The two groups of patients were compared as to rate of roentgenographic stabilization, sputum conversion, and cavity closure. Stabilization was defined as that point following which, in retrospect, roentgenograms remained unchanged, with or without cavity present, for at least three months without surgery. Of the control patients 38 "stabilized" roentgenographically. The average time from beginning of therapy to point of stability was 6.9 months, and in 10 months 89% had reached stability. In the study group, 21 of whom "stabilized" without surgery, the mean stabilization time was 7 months, and 93% stabilized without surgery in 10 months or less (fig. 1). (Difference of means=0.1 months; standard error of means=1.5.)

TABLE 3.—*Chemotherapy Received**

	Nonpregnant		Pregnant	
	No.	%	No.	%
Isoniazid and streptomycin	12	30	5	23
Isoniazid and para-aminosalicylic acid	7	17.5	8	37
Streptomycin and para-aminosalicylic acid	9	22.5	2	9
Isoniazid and streptomycin and para-aminosalicylic acid	12	30	7	32
Total on isoniazed	31	77.5	20	91

* The difference in regimens is based on the fact that the streptomycin and para-aminosalicylic acid regimen was in vogue at the earlier part of the time period covered rather than on any effort by the physician to give more potent treatment to the pregnant patients.

As will be noted below some patients in both groups ultimately underwent surgery. However, in almost all cases chest x-rays had shown no significant changes for at least three months prior to surgery, and patients whose x-rays "stabilized" after surgery are not included in these figures.

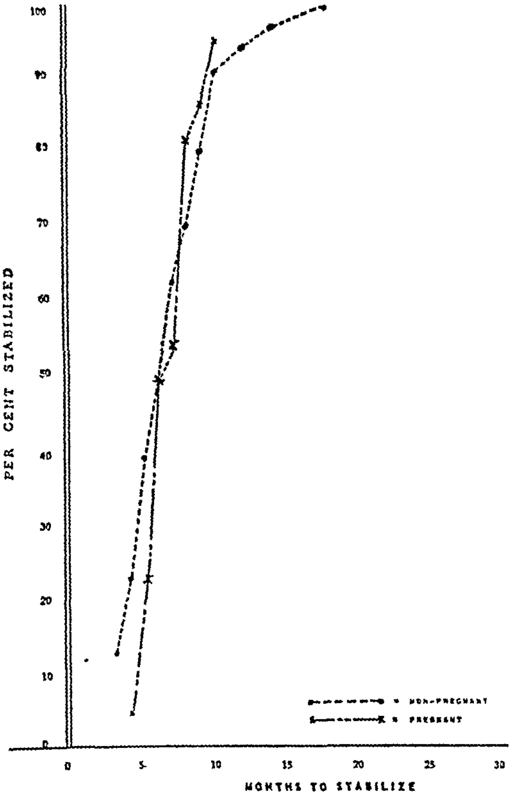

Fig. 1.—Rate of stabilization of disease.

Figure 2 depicts graphically the rate of conversion of sputum (or gastric contents) after the beginning of drug therapy. After five months results of tests on 95% of the pregnant group and 92% of the control group were negative for bacilli and remained so thereafter. Figure 3 shows the rate of cavity closure in the two groups. In most cases failure of cavities to close after six months of chemotherapy was regarded as an indication for surgery, unless other contraindications existed. Patients who agreed to operations were generally operated on between the 7th and 10th month; hence, evaluation of this parameter could not be extended beyond 7 months. Of 13 initially cavitary patients in the study group in 7 (54%) the cavities had closed by seven months; of 24 initially cavitary controls in 13 (54%) the cavities had closed. In none of these areas of evaluation is there a significant difference between control and pregnant patients.

Seven nonpregnant patients were discharged with active disease, in one of whom the disease was found inactive on follow-up examination; two had "open negative" cases which are still stable; and two had cases that became "open negative" during follow-up. One patient was rehospitalized elsewhere because of relapse, and one was lost to follow-up. Of three patients discharged with active disease in the pregnant group two were lost to follow-up and in one the disease is "open negative" and has remained stable for over a year. An operation is planned in this last case after delivery.

Eight patients in each group had resectional surgery after seven months or more of chemotherapy for persistent residual disease or cavitation.

There were 11 nonpregnant patients in whom cavity closure did not occur after seven months of rest and chemotherapy; 5 of these had operations, 4 retained their cavities with roentgenographic stabilization and persistent negative sputum for six or more months, and 2 were lost, having left against medical advice. Of the six pregnant patients whose cavities did not close three had operations at seven months, in one the disease is stable and "open negative," and two left the hospital against medical advice.

The obstetric results in the pregnant patients were excellent; 21 had full-term, normal, uncomplicated deliveries of healthy babies. One of these subsequently had another child with continuing stability of her disease, and one is presently undelivered and "open negative." Among the control group there have been four pregnancies after discharge from the hospital. Two have delivered, and have been examined over a period of 18 months subsequently; two others (with inactive disease

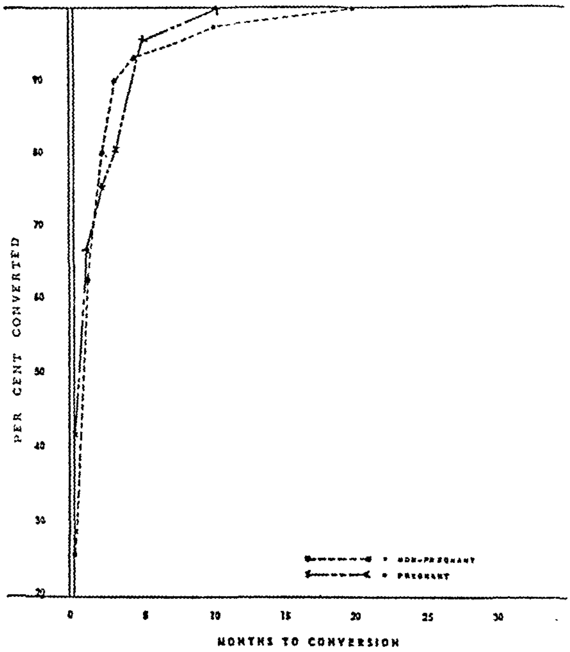

Fig. 2.—Rate of conversion of sputum and gastric secretions.

for 7 and 17 months, respectively) are currently pregnant. There has been no evident change in the status of their tuberculosis.

Comment

The problem of pregnancy in tuberculosis up to the beginning of the chemotherapeutic era has been well reviewed by Hedvall.[2] Briefly, he noted that since the time of Hippocrates pregnancy had been thought beneficial to the phthisis until about 1850, when medical opinion began to suggest an unfavorable course of tuberculosis complicated by pregnancy. By 1924 the concept of induced abortion, as a means of coping with the dire import of tuberculosis in pregnancy, became widespread. Hedvall cited series totaling over 1,000 cases purporting to show the adverse effect of pregnancy on the course of tuberculosis. He also noted a similar group of reports which showed a neutral or favorable relationship. He reviewed conflicting reports on the course of tuberculosis in pregnant experimental animals. In 250 mothers in his own study there were 24 abortions and 346 full-term pregnancies. He found no significant change during pregnancy, some (9.1%) having improved and some (7%) having worsened. He noted similar results in improvement and worsening in the first postpartum year. Giercke[3] presented similar results in a series of 930 pregnancies. In the United States Rosenbach and Gangemi[4] noted deterioration in the conditions of many pregnant patients who had active tuberculosis without adequate treatment. All of these reports suffer from a failure to state clearly the extent of the disease, activity of the disease in relationship to the time of pregnancy, and treatment received.

Raeburn and Clancy[5] reviewed 41 pregnant hospitalized patients with active tuberculosis. All improved while awaiting confinement and in the puerperium and received chemotherapy only in the puerperium. There are reports of postpartum relapse.[6] Cromie[7] noted that in 101 pregnancies, 20 of 31 relapses occurred in the first postpartum year. However, Stewart and Simmonds[8] in studying the tuberculosis reports for England found that the five-year survival rates had no relationship to pregnancy and that women pregnant within 18 months of a case of active tuberculosis had no worse outcome on five-year follow-up examination. Edge[9] showed that in England, while there is no greater incidence of tuberculosis in pregnant women than in the general population, there is a lower birth rate among women who have had tuberculosis.

Williams[10] reported a series of 16 patients who had full-term normal deliveries after thoracic surgery for tuberculosis. Corner and Nesbitt[11] reported another 47 cases of delivery after pulmonary resection and presented 15 cases of their own showing that women who have had lung surgery do well obstetrically. Furthermore, of six patients operated on during gestation they noted one abortion, one death due to empyema, and four uncomplicated deliveries. Schaefer and Epstein[12] also reported two cases of patients who did well who had had surgery during pregnancy.

Therapeutic abortion for tuberculosis is infrequent today. Schaefer[13] showed that of 41 patients with far-advanced cases who had therapeutic abortions in the first trimester, only 17% improved, as compared to 49% showing improvement of 43 patients with similar cases who were allowed to go on to full term. Other reports have also suggested that abortion has little to offer in the therapy of tuberculosis.[14]

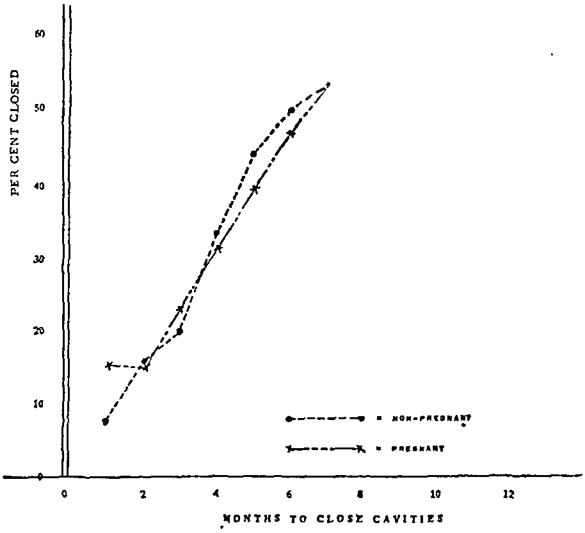

Fig. 3.—Rate of cavity closure.

The present series is limited by its small numbers. However, in a small group of women with similar background data, all of whom had active pulmonary tuberculosis, there was no difference in response to chemotherapy for tuberculosis in pregnant women as compared to nonpregnant women.

Summary

In a series of 22 pregnant patients with active tuberculosis compared to 40 nonpregnant patients with comparable background data, there was no statistical difference in rate of bacteriological conversion, roentgenographic stabilization, or cavity closure. All but one of each group were original treatment cases.

The results indicate that pregnancy does not alter the tuberculosis prognosis, provided the disease is treated the same as that disease not complicated by pregnancy.

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VALSALVA MANEUVER AS A DIAGNOSTIC AID

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The test for cardiac function here described consists of having the patient blow into a manometric system in such a way as to maintain an intrapulmonic pressure of 40 mm. Hg for 10 seconds. During and immediately after this straining period the patient's blood pressure is noted. A four-phase response, consisting of a brief rise of 30 to 50 mm. Hg in systolic blood pressure, a gradual fall to resting level, a brief fall below resting level when the strain is released, and a secondary rise of 15 to 40 mm., is considered a normal response. The test was applied to 205 selected office patients. Positive results (abnormal responses) were obtained in 35. Of these, 14 showed clinical signs of congestive heart failure and 11 had significant heart disease.

The Valsalva maneuver as a test for cardiac function[1] is a simple procedure requiring no expensive or complicated equipment. The test can be done within a few moments at the patient's bedside with material readily available in any hospital or physician's office. In spite of the paradox of ease of testing and availability of materials, the results are usually clear-cut and of significant value to the practicing physician in evaluating the complaint of shortness of breath. The use of this maneuver is a practical method of study with some positive benefits to the examiner, as congestive heart failure has been found to produce a pattern almost diametrically opposed to that of emphysema.[2] It is also of interest that no patients were found to be unable to complete the test except those obviously very feeble from age or illness and those with psychological dyspnea. In addition, the presence of auscultatory findings of valvular heart disease requires meticulous evaluation, in this modern era of cardiac surgery, and a bedside test[3] giving helpful information is urgently needed. Dynamically significant mitral and aortic stenosis appear to give abnormal responses, and, if more study confirms the results, this test will be of distinct value. Some do not believe the test is of value[4] in valvular obstruction, but this disagreement may be due, in part, to technique.

Because of the desire to further evaluate the procedure in private practice, 205 selected office patients were tested and evaluated. No patients initially seen in the hospital were included in this study, although the test was performed on many of these patients.

Materials and Methods

The test was performed during the routine complete physical examination given every new patient examined. This included, besides the complete history and physical examination, a complete blood cell count, urinalysis, Wassermann test, corrected sedimentation rate determination, and fluoroscopy of the heart and lungs. Electrocardiograms were done where indicated and on all men over 35 and women over 40 years of age. Other studies, such as ballistocardiography and vital capacity, were done where necessary. Many of the patients were later hospitalized and more completely studied.

The test was performed in the following manner: A 2-oz. Asepto syringe was connected by a short piece of rubber tubing to an aneroid manometer taken from a Tycos sphygmomanometer. With the patient resting in a supine position, the blood pressure was obtained and allowed to become stable. The patient was then instructed to blow quickly into the syringe from a moderate inspiratory position. Usually with one or two trials the pressure could be raised 40 mm. Hg and maintained for 10 seconds. The blood pressure was watched and noted both during and after the straining period. With practice this is easily done, and not only can the levels of systolic pressure be observed but some gross estimate of the pulse pressure and pulse can be obtained.

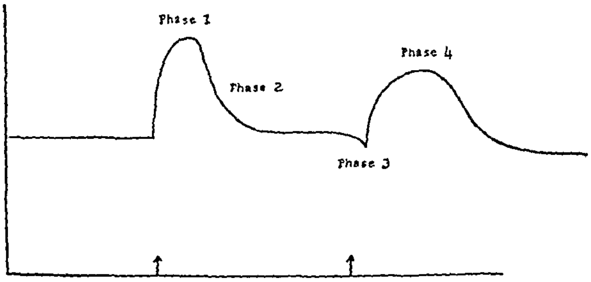

Fig. 1.—Normal Valsalva response, showing changes in systolic blood pressure during 10-second period of straining (*between arrows*). Note rise in pressure on straining (phase 1), drop in pressure (phase 2), fall below base line (phase 3), and poststraining rise (phase 4).

A normal response (fig. 1) is an abrupt rise (phase 1) in systolic pressure of 30 to 50 mm. Hg lasting less than 5 seconds and usually only 1 or 2 seconds. This is followed by a gradual fall to the resting level until straining is released (phase 2). On release of straining, an abrupt, momentary fall in blood pressure occurs (phase 3) which is followed by a secondary rise of pressure to levels of 15 to 40 mm. Hg above the base line (phase 4). Bradycardia and gradual return to the steady state then occurs.

If the examiner "sets" his blood pressure cuff to approximately 30 mm. Hg above the resting systolic level just prior to straining, he will usually have no difficulty in observing the first phase. The systolic blood pressure can then be followed during the next 10 seconds and, if the usual fall occurs, the pulse pressure can be estimated toward the end of the straining period. On release of straining, the cuff is again quickly inflated to 20-30 mm. Hg above resting level (during the third phase), and the poststrain rise is easily noted. Others do not attempt to "follow" the blood pressure during the period of 10 seconds but raise the cuff pressure to 20-30 mg. Hg above resting systolic pressure with the onset of straining, leave it there during straining, and then listen to the Korotkoff sounds for the poststraining overshoot. This is less cumbersome but does not allow the observation of the exaggerated normal response seen in emphysema. The following important aspects of the maneuver can therefore be easily observed: 1. Was there a rise on straining? 2. Did the usual drop in blood pressure occur during the second phase? 3. Was there a significant fall below the base line? 4. Was there a normal poststraining rise or overshoot?

Few difficulties were encountered after the procedure became familiar to the examiner. All of the patients who originally showed false-positive results, and who were retested, finally showed normal results, but, unfortunately, several patients who did give an abnormal response could not be reexamined. The most frequent technical errors noted were excessive inspiration prior to straining and straining from a midposition or almost expiratory position. The patients will almost invariably strongly inspire when asked to strain, and, when cautioned against this, some will attempt to strain almost from the expiratory phase. In addition, the initial onset of straining must be abrupt and the pressure quickly brought to 40 mm. Hg or the first phase will not occur. The presence of auricular fibrillation makes it quite difficult to be accurate in measuring the levels of pressure and usually makes it impossible to perform the test. I had no trouble with the few patients I observed, but the number was small and the rhythm slow and almost regular in these.

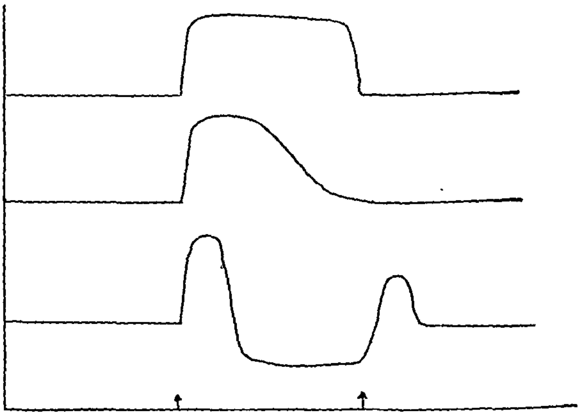

Fig. 2.—Abnormal Valsalva responses, showing changes in systolic blood pressure during 10-second period of straining (*between arrows*). *Top,* typical response in patient with congestive heart failure. *Center,* response of patient with some congestive heart failure and/or dynamic obstruction of valve. *Bottom,* response of patient with emphysema.

In the patients with congestive heart failure an entirely different type of response occurred (fig. 2). After the onset of straining the systolic blood pressure rose to 30 to 40 mm. Hg above resting level and persisted for more than six seconds, usually throughout the period of straining. In addition, the poststraining rise did not occur. The response of

Congestive Heart Failure

Case No.	Age of Patient	Condition	Congestive Heart Failure		Remarks
			Yes	No	
5	17	Rheumatic heart disease, mitral insufficiency, questionable mitral stenosis	...	X	Functional, class 1
10	36	Psychoneurosis	...	X	Rechecked and normal
20	31	No disease	...	X	Rechecked and normal
21	27	Idiopathic pulmonary hypertension	...	X	Cardiac catheterization, three times; asymptomatic for 3 yr.
27	73	Coronary artery disease, angina pectoris	X	...	...
28	32	No disease	...	X	Normal on recheck
29	33	Rheumatic heart disease, mitral stenosis, mitral insufficiency	X	...	...
31	35	Coronary artery disease	X	...	...
37	36	Coronary artery disease, left ventricular aneurysm	X	...	...
45	52	Psychoneurosis	...	X	Normal on recheck
46	39	Rheumatic heart disease with mitral stenosis	...	X	Refused surgery
49	43	Rheumatic heart disease, aortic stenosis, postoperative aortic insufficiency	X	...	Borderline abnormal
52	42	Thyrotoxicosis, auricular fibrillation	X	...	Reverted to normal sinus rhythm, and test became normal postoperatively
61	27	No disease, obesity (weight 228 lb. [103.4 kg.]; height 5 ft. 11.5 in. [180 cm.])	...	X	Valsalva normal at 60 mm. Hg
64	25	No disease, questionable mitral stenosis	...	X	...
69	51	Coronary artery disease	X	...	Possible left ventricular aneurysm
84	21	Congestive heart disease, pulmonary stenosis	...	X	...
99	40	Aortic regurgitation of questionable cause	...	X	Probably syphilitic
100	72	Pulmonary fibrosis and emphysema	X	...	Probable coronary artery disease; died
103	62	Coronary artery disease	X	...	Became normal with drug therapy
108	28	Congenital heart disease, Eisenmenger complex, cyanotic, severely limited	...	X	Diagnosis proved by cardiac catheterization
115	52	Coronary artery disease, left ventricular aneurysm	...	X	All tests for congestive heart failure were normal-asymptomatic
117	54	Coronary artery disease	X	...	...
118	66	Coronary artery disease	X	...	Cleared with drug therapy
119	70	Emphysema	X	...	Probable coronary artery disease, died
133	35	No disease (hiatus hernia), obesity (199.5 lb. [90.9 kg.])	...	X	Normal after 35 lb. (16 kg.) weight loss on recheck
139	22	Rheumatic heart disease with 2+ aortic insufficiency, 2+ mitral stenosis, and 2+ enlarged left ventricle	...	X	Borderline abnormal test with slow fall, second phase only; normal overshoot
146	42	High blood pressure, postsympathectomy, blood pressure 180/110 mm. Hg	...	X	Typical response for sympathectomy with no overshoot or bradycardia
151	43	No disease	X	...	...
152	61	Hypertension	X	...	Probable early failure, cleared on drug therapy
169	11½	Congenital heart disease, aortic stenosis	...	X	Child is not limited
184	59	Severe congestive heart failure, unknown cause	X	...	Remains abnormal though clinically out of failure
188	47	Coronary artery disease, Stokes-Adams syndrome	...	X	Died within 2 mo., test became normal on rest and digitalization
193	54	Carcinoma of lung with superior mediastinal syndrome	...	X	Died within 3 wk.
209	39	Rheumatic heart disease with aortic stenosis	...	X	...

the patient with uncomplicated emphysema was quite dissimilar to that described above and more nearly like that of a supernormal response. A sharp rise in pressure occurred at the onset but was quickly followed by a deep fall in pressure to a point below the resting level. Pulse pressure at this point seemed to be quite narrow. The usual fourth phase rise then appeared. In patients with dynamically significant mitral and aortic stenosis the pattern is similar to that of congestive heart failure, although most interest has centered on the failure of the overshoot to appear. The clinician may not be able to distinguish between the two patterns at the bedside, but this is of little practical importance or necessity.

Many patients with hyperventilation syndrome and psychological dyspnea were unable to exert sufficient force to satisfactorily perform the test.

Results

In the 205 patients tested, 35 positive tests occurred (see table). Of these, eight were felt to be cardiovascular normals. Six of the eight patients were rechecked, and all gave a normal response. This result was attributed to technical errors overcome in becoming more proficient with the procedure; the other two patients, if they could be retested, probably would also give normal responses.

Fourteen patients were felt to be in definite congestive heart failure. Although the symptoms were of varied cause, all patients gave abnormal responses to testing, but some returned to normal on treatment. These include two patients with severe chronic pulmonary emphysema and fibrosis.

Thirteen patients who were not in evident heart failure were found with abnormal congestive failure type test results. Of these, 11 had significant heart disease. These included two with aortic stenosis, one with mitral stenosis, one with mitral insufficiency, two with aortic regurgitation, one with idiopathic pulmonary hypertension, one with congenital pulmonary stenosis, and one with Eisenmenger complex. All of these were clinically severe forms of heart disease, and the presence of an abnormal test result is not unexpected or surprising.

The single postsympathectomy case encountered was in a 42-year-old male with moderate residual hypertension and with no evidence of congestive heart failure or limitation of activities. His test results were as would be expected, with an immediate first phase rise but no poststraining rise or bradycardia.

The patient with a Stokes-Adams seizure due to paroxysmal ventricular tachycardia did not show clinical evidence of congestive heart failure. Because of the abnormal response, he was digitalized, and when the test was later repeated it was normal. He did not, however, lose weight on therapy and died suddenly after six weeks.

lar heart disease is strongly suggestive of congestive heart failure. The presence of an abnormal response in valvular heart disease, with particular reference to aortic and mitral stenosis, suggests dynamically significant obstruction of the valve orifice. The presence of an abnormal response in a patient with emphysema suggests concurrent congestive heart failure or other abnormalities of the pulmonary vascular bed.

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TODAY'S PATIENT.—The 1955 model of patient is a different individual than the 1935 model. The later model is a better educated person and much better informed about medical matters because of medical columnists, magazine articles, books, radio, and television. If he watches "Medic" on television he may even know how to operate. The gripes twenty years ago were that the other fellow did not cure him or at least not fast enough. The gripes of today are different. He tells you that the other fellow did not take any interest in him, was completely impersonal, hurried him through, told him there was nothing wrong with him, did not explain things to him or used medical jargon, and charged him too much. In brief, he looks upon us as scientists and mechanics and not as physicians in the true sense of the word. He would like to have sympathy and understanding in addition to the magic medicines and spectacular techniques; in other words, to be considered as more important than his disease. . . . The patients with mild neuroses are one of the most fertile sources of misunderstanding and dissatisfaction. . . . They really resent being told that there is nothing wrong with them and of course if there was nothing wrong they would be somewhere else and not in your office. It has been stated that about 50% of the patients coming to physicians today have troubles that are of psychosomatic origin. Since about 3% of the doctors are psychiatrists, obviously it is impossible to pass them all on. . . . All specialists should take care of their own neurotics. It is mainly a job of taking plenty of time and listening. . . . Since I got interested in this subject I have made it a point to spend 5 to 15 minutes extra with the patient who is mildly neurotic and the expressions of gratitude and confidence are quite amazing. . . . Then too, we should remember that if the patient does have serious pathology the psychic effect of the disease on the patient may be as important as the disease itself. Patients go to the cultists mainly because they are friendly and will listen.—W. J. Butler, M.D., Public Relations and the Patient, *The Journal of the Michigan State Medical Society*, December, 1958.

A most interesting case (case 115) in which there was an abnormal response was that of a patient having a moderately large, left ventricular aneurysm of several years' duration. The patient presented no findings of active coronary artery disease or of congestive heart failure. It is interesting to speculate as to the cause of this false-positive response in an asymptomatic patient.

One patient with carcinoma of the lung and superior mediastinal syndrome died within three weeks of testing, with a very rapid, down-hill course; autopsy showed no evidence of heart disease. Another patient with superior mediastinal syndrome due to carcinoma gave a normal test result in spite of a previous coronary occlusion and myocardial infarction.

Emphysema was encountered in 11 patients during this study. Two of these are included in the abnormal group and both died. Four of the remaining nine were seen prior to my being aware of the emphysema response, as described by Mills and Kattus,[2] and were recorded as having a normal response. The remaining five all showed an exaggerated normal response. The magnitude of this response is usually fairly marked, but these patients were too few in number for further conclusions to be drawn, except to note that both of those with emphysema showing an abnormal response of the congestive failure type died within a short period of time.

Of the 205 patients there were 11 who were unable to complete the test. Of this number, seven were psychoneurotics without organic disease. Three others were elderly, feeble patients, one of whom was unable to "blow" because of a paralyzed lip. Studies in many other such patients were subsequently not attempted. The only patient with organic disease tested who was not able to complete the procedure was a neurotic male aged 64 with probable mitral stenosis. As his exercise tolerance was not significantly limited, it was felt that his "neurosis" was more important than the organic disease.

There were 150 patients encountered with a normal response. This number included 125 felt to be cardiovascular normals, although a relatively large number of these had asymptomatic coronary artery disease or hypertension. None of these had cardiomegaly or any clinical evidence of congestive heart failure. In addition, there were 16 patients with coronary artery disease with varying degrees of mild angina or who had recently had a coronary occlusion. No patient was tested in the immediate postinfarction period, and none were felt to be in congestive heart failure. In addition, there were three cases of mitral stenosis, two of aortic stenosis, and one each of hypertension with aortic regurgitation (probably syphilitic), chronic nonconstrictive pericarditis, hyperthyroidism, and superior mediastinal syndrome due to carcinoma.

Some of the patients with normal responses were of great interest, and many underwent more detailed study. For example, one of the group with aortic stenosis had normal findings at left heart catheterization, and this finding of a normal gradient across the valve should exclude stenosis as the cause of his symptoms. One of the patients with mitral stenosis was pregnant, and repeated normal tests throughout her gestation were most reassuring. No patient with a normal response was found to be clinically in congestive heart failure, and all patients with valvular disease and a normal response were felt to be clinically in functional class 1, except for the patient with aortic stenosis, as noted above.

Comment

Although the Valsalva maneuver was described many years ago, and intermittent interest has been shown in the test over a number of years, it is only recently that its advocation as a clinical test has appeared. Hamilton and others,[5] in 1944, studied the physiology of this maneuver, but it was not until recently that Sharpey-Schafer,[6] Gorlin and others,[1a] Knowles and others,[1b] Greene and Bunnell,[3b] Ard and Twining,[1c] and Goldberg and others [3a] have shown interest in the test as a clinical procedure. Originally, interest in the overshoot occurring during the fourth phase was most intensely studied,[1f] and this apparently depends on the effects of reflex vasoconstriction. The single case in the present study of a patient after sympathectomy confirmed previous reports of this nature.[7] The drop in blood pressure during the second phase, however, seems more dependent on cardiac function itself and has been extensively studied. Stenosis of mitral and aortic valves produces abnormalities in response by obstruction to the flow. It is for this reason that its use in preoperative investigation urgently needs further study. It is beyond the scope of this paper to discuss the physiological principles involved, and the reader is therefore referred to the excellent reviews recently published.[8]

It is possible, after use of the maneuver in clinical practice, to draw some conclusions, and I feel that because of the simplicity of the test it should be included in the armamentarium of every practicing physician.

Conclusions

The Valsalva maneuver as described is a simple procedure, easily performed in the physician's office or at the bedside, giving significantly accurate results in the majority of cases. A normal response would appear to be extremely rare in the presence of congestive heart failure and was not encountered in a single case in this study. False-positive tests in normal patients rarely occur, but the number can be significantly reduced as the proficiency of the operator increases. The presence of an abnormal response in a patient with dyspnea without valvular heart disease is strongly suggestive of congestive heart failure. The presence of an abnormal response in valvular heart disease, with particular reference to aortic and mitral stenosis, suggests dynamically significant obstruction of the valve orifice. The presence of an abnormal response in a patient with emphysema suggests concurrent congestive heart failure or other abnormalities of the pulmonary vascular bed.

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COMPLETE CORRECTION OF THE TETRALOGY OF FALLOT BY OPEN-HEART SURGERY

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In patients with the tetralogy of Fallot, open heart surgery has advantages over the palliative operations permitted by older techniques because it is generally able to correct the underlying defect of the interventricular septum. This report concerns 10 consecutive patients in whom the defects were completely corrected with use of a heart-lung machine capable of oxygenating and delivering more than 5 liters of blood per minute. Details of anesthetic and surgical procedure are given. The period of cardiopulmonary bypass lasted from 22 to 49 minutes. There was one operative death. The nine other patients showed striking improvement. Most striking was that seen in a woman, aged 32, formerly a bedridden invalid, who after operation was able to do her own housework and work full time as a saleslady. Since further reduction of operative mortality is anticipated, the new technique greatly improves the prognosis of patients with the tetralogy of Fallot.

In 1945, Blalock and Taussig[1] reported their first three successful cases of tetralogy of Fallot treated by anastomosing the proximal end of the subclavian or innominate artery to the side of the pulmonary artery. This was the first time that the patient with tetralogy of Fallot was treated with surgery. Up to this time blue babies with malformed hearts were beyond surgical treatment. This monumental work marked the beginning of the surgical treatment of tetralogy of Fallot.

The tetralogy of Fallot is a syndrome which is characterized by four specific changes in the heart. There is a ventricular septal defect, overriding of the aorta, pulmonary stenosis (infundibular, valvular, or both), and resultant hypertrophy of the right ventricle. The cyanosis in these patients is due to the admixture of blood from the right ventricle shunting through the ventricular septal defect into the aorta. The more severe the pulmonic stenosis and the larger the defect, the greater the shunt from the right ventricle into the aorta and the more cyanotic the patient.

In 1946, Potts, Smith, and Gibson[2] reported on the first three patients on whom they performed a side-to-side anastomosis between the aorta and the pulmonary artery for the treatment of tetralogy of Fallot. This operation was patterned after the Blalock procedure and was also intended to increase the flow of blood to the lungs.

In 1952, Taussig and Bauersfeld[3] reported on the first 1,000 patients operated on at the Johns Hopkins Hospital for the treatment of pulmonary stenosis. In those patients in whom the preoperative diagnosis was tetralogy of Fallot, there was a 15% operative mortality with the Blalock procedure.

As recently as 1958, there have been reports of surgeons still employing the palliative procedures such as the Blalock procedure and the Potts procedure instead of open-heart surgery for the complete correction of tetralogy of Fallot. In August, 1958, Moss and associates[4] reported a 9% immediate mortality with the older shunt procedures for the treatment of tetralogy of Fallot.

In 1956, Lillehei and co-workers[5] reported on 29 patients who were operated on for tetralogy of Fallot, with use of open-heart surgery. These 29 patients had a corrective operation which consisted of closure of the ventricular septal defect, correction of the overriding of the aorta, and resection of the infundibular stenosis or pulmonary valvotomy. Of these 29 patients, 20 lived. There was, therefore, a 33% mortality.

The following report concerns our first 10 consecutive patients with tetralogy of Fallot operated on with complete correction of their defects, with use of the Kay-Anderson heart-lung machine. The heart-lung machine used incorporates two roller pumps and a stainless steel autoclavable stationary screen oxygenator which is capable of oxygenating and delivering over 5 liters of blood per minute. A complete description of this equipment[6] and its use in closure of ventricular septal defects[7] has been previously reported.

The patients operated on for tetralogy of Fallot were 2½ to 32 years of age and weighed from 28 to 152 lb. (12.7 to 68.9 kg.) (see table). In all cases there was a history of continuous or intermittent cyanosis, dyspnea, severe fatigue, and decreased exercise tolerance. Three of the 10 patients had been observed to squat. Cough, respiratory infec-

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From the Cardiovascular Research Laboratory, departments of surgery and medicine at the University of Southern California School of Medicine, St. Vincent's Hospital, and the Los Angeles County Hospital.

tions, and epistaxis were frequent. The 32-year-old woman was bedridden, and the remaining patients were severely limited in exercise tolerance.

The physical findings were typical of tetralogy of Fallot and included cyanosis, clubbing of the fingers and toes, and a systolic murmur at the pulmonary area and at the fourth left intercostal space. In some of the patients a systolic thrill was also present at the fourth left intercostal space. Four patients had decrease in growth rate and five had bony deformity of the chest, such as pigeon breast. Asymmetry of the chest was common in these 10 patients. Electrocardiograms uniformly were reported as showing right ventricular hypertrophy. X-rays revealed enlargement of the right ventricle with decreased pulmonary vascular markings. Five patients showed minimal enlargement of the main pulmonary artery. Right heart catheterization revealed right ventricular pressures ranging from 76/6 to 160/3 mm. Hg, with pulmonary artery pressures much lower in each case, being 20/10 to 50/20. Femoral artery oxygen saturation ranged from 57% to 96%.

Open-Heart Surgery on Ten Patients with Tetralogy of Fallot

					Cardiac Catheterization (Pressures and Saturation)											
					Right Atrium		Right Ventricle		Pulmonary Artery		Femoral Artery					
Case	Age, Yr.	Wt., Lb.	Clinical Manifestations	Cyanosis	Mm. Hg	%	Mm. Hg	%	Mm. Hg	%	Mm. Hg	%	Stenosis	Septal Defect, Cm.	By-pass, Min.	Result
1	7	52	Dyspnea, pneumonia 3 times, epistaxis, squatting	After exercise	20/10	71	120/15	71	30/20	71	150/90	96	Infundibular	1.6	22	Excellent
2	4	32	Shortness of breath, cough, no squatting	Severe with crying	11/6	43	105/0	57	Not entered		105/67	79	Valvular	3	49	Part of valve removed because of severe stenosis
3	32	152	Pronounced dyspnea	Severe, constant	5/0	51	130/0	46	20/10	45	105/30	57	Infundibular	2.5	36	Excellent
4	3½	28	Dyspnea, tiredness	With exercise	...	66	119/0	65	13 mean	66	119/70	84	Infundibular	3	33	Excellent
5	10	43	Severe colds	Blue spells	...	59	76/6	60	37/17	64	72/30	80	Infundibular	3	29	Excellent
6	2½	29	Tiredness, dyspnea	Constant	4/0	58	100/3	60	Not entered		100/60	75	Valvular, bicuspid	3	22	Developed complete heart block: died on table
7	10	65	Respiratory infection, pneumonia, shortness of breath, cough, weakness	Episodes	15/10	59	140/15	65	50/20	71.5	150/90	87	Valvular, tricuspid	3	49	Excellent
8	3	34	Dyspnea, no syncope, squatting	Constant, severe	20/14	55	120/20	60	Not entered		150/95	64	Infundibular	2	44	Excellent
9	13	91	Shortness of breath, colds, tiredness, squatting	Constant episodes, severe	4/0	67	160/3	66	28/12	65	160/75	82	Infundibular	3.5	40	Excellent
10	5	47	Shortness of breath, decreased exercise, no cyanosis	0 to 1+	4/0	65	100/5	64	15/4	65	100/58	86	Infundibular	2	37	Excellent

Anesthesia was managed and maintained in so light a plane that the patient was awake at the end of the procedure. Whenever feasible, hypnosis was used for induction. In only two patients was preoperative medication used and this consisted of administration of a small amount of scopolamine. The rest of the patients received no preoperative medication.

The anesthetic agents used were cyclopropane for the first few minutes, followed by nitrous oxide and oxygen and endotracheal intubation. Succinylcholine was used as the muscle relaxant throughout until the end of the bypass. After cardiopulmonary bypass only nitrous oxide and oxygen was used. Advantage was taken of the hypothermia developed during bypass to maintain amnesic analgesia. Neither the blood nor the patient was rewarmed during bypass. After bypass the patient rewarmed spontaneously. During bypass, helium and oxygen (60:40%) was used to gently inflate the lungs. After bypass, manual ventilation was resumed with 100% oxygen or 50% nitrous oxide and 50% oxygen.

Procedure and Results

In the early cases a bilateral anterior thoracotomy was used but this has been replaced by a median sternotomy which is less painful postoperatively and decreases pulmonary complications.

After cardiopulmonary bypass was started, a 7 to 10 cm. right ventricular incision was made from just below the pulmonary valve toward the right ventricular apex. The infundibular stenosis was circumferentially excised until an adequate outflow tract was obtained. When present, pulmonary valvular stenosis was corrected by cutting the fused commissures through a separate incision in the pulmonary artery. This incision gave better exposure to the valve than an incision in the right ventricle.

A normal valve was restored in all but one patient (case 2). In this patient a diaphragm was present instead of well-formed cusps. The ventricular septal defect was closed, primarily with interrupted figure of eight 2-0 silk sutures (nine cases). A compressed Ivalon sponge patch was necessary in the other case. No pulmonary outflow tract patches were needed. Overriding of the aorta was automatically corrected by closure of the septal defect.

The postoperative course was benign and uneventful in all patients except the 32-year-old woman, who had congestive heart failure on the fifth postoperative day and required a tracheotomy for better ventilation. She was also digitalized at this time. The end-result in this case, however, was excellent despite this episode of failure. At the time of writing, nine months after operation, she was not restricted in any fashion. She leads a normal life and is no longer on digitalis therapy or a cardiac regimen.

One death occurred in the only patient having potassium ion cardioplegia. Complete heart block resulted from the septal defect closure and contributed to her death in the operating room. Heart block was prevented in the other cases where the heart was not stopped by observing the electrocardiogram during the placement of each suture and replacing any stitch which altered the conduction pattern. The duration of cardiopulmonary bypass was 22 to 49 minutes in the 10 patients.

The most striking improvement observed was in the patients most handicapped before surgery, as all of the nine are now normal in exercise tolerance and arterial oxygen saturation. The oldest patient before surgery was a bedridden invalid. She now not only performs her own housework but works full time as a saleslady. She, however, is also impressed with her beautiful pink complexion. This is characteristic of the psychological improvement after correction of this organic defect. The most incapacitated child now plays and exercises in a normal manner.

Conclusions

Ten patients with tetralogy of Fallot had anatomic correction of their defects, with only one death. With this low mortality, complete correction of the tetralogy of Fallot would appear to be preferable to shunting procedures.

2122 W. Third St. (57) (Dr. Kay).

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The heart-lung machine used in this study was constructed by Corco, Inc., Los Angeles.

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CAUTION IN THE INDUCTION OF LABOR.—In all inductions of labor careful selection of candidates and strict adherence to technique will greatly reduce the number of complications, or reduce their severity to a degree that will not result in serious tragedy for mother or infant. . . . If it is not possible to observe these precautions, the induction of labor should not be attempted. If, for medical obstetrical reasons, the pregnancy must be terminated, a Cesarean section would be safer for mother and infant than a poorly conducted induction of labor.

The important considerations in assuring the success and safety of an elective induction are: 1) suitable selection of the patient as to the ripeness of the cervix and maturity of the infant; 2) constant attendance by an experienced person as long as the oxytocin is running; 3) experience in the technique of amniotomy; 4) adequate facilities for coping with any of the potential complications; and 5) in indicated inductions, a medical or obstetrical condition that requires termination of pregnancy with no great urgency. When these criteria are met, and adherence to technique is strict, induction of labor may be practiced with confidence for the successful delivery of the infant and with complete safety to the mother. More work must be done in this field before the induction of labor can be freely recommended for general use. The personnel and technical requirements are such that it is doubtful that this procedure will ever become sufficiently innocuous to permit its widespread use, except in the hands of experienced obstetricians who are practicing in well equipped hospitals with completely adequate personnel to carry out the rigid technical requirements.—Harry Fields, M.D., The Present Status of Induction of Labor, *Delaware State Medical Journal*, April, 1959.

THE HANDS IN ARTHRITIS

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In cases of rheumatic disease special attention should be given to the patient's hands. They are readily examined for manifestations of the disease, and their usefulness is seriously impaired by the resultant deformity. Medical measures include use of salicylates, phenylbutazone, and the steroids for their anti-inflammatory effect. Physical measures include diathermy, paraffin baths, whirlpool baths, ultrasonic treatment, massage, and exercise. Both passive and active exercises for the hand can be performed in a basin of heated water. If a patient is willing to cooperate by spending one or two periods each day in self-treatment he can carry out some of these forms of physical therapy in his own home with considerable benefit.

The purpose of this paper is to bring to the attention of physicians the importance of the hands in the study of rheumatic diseases. From the economic standpoint the hands are the most important members of the body. A person without sight, without hearing, or even without the use of his lower extremities is usually able to earn a living provided his hands remain in a normal or relatively normal condition. The loss of the use of the hands, however, forces the victim to be dependent on others for his livelihood, regardless of what other faculties remain intact.

From the diagnostic standpoint the hands are usually affected early and with distinguishing features in most of the rheumatic diseases; they are readily observed and easily examined. From the therapeutic standpoint the hands are often neglected, yet they lend themselves easily to treatment and, if this treatment is properly given, excellent results are usually obtained.

Motions of the hands fall into three general categories. The first of these is "gripping," performed by holding an object between the flexed fingers and thumb, all of the phalanges being used to support the object grasped. This is the function used in lifting a glass of water to the mouth or in using a hammer or saw. The second basic function of the hands is "pinching," in which an object is held between the distal phalanges of the thumb and one or more fingers. Most characteristically this is involved in use of a needle, but minor variations occur in holding a pen or spoon. Cutting food with a knife is a combination of these first two maneuvers. The third basic function of the hand is "tapping," in which the principal motion occurs at the metacarpophalangeal articulations (and to a lesser extent at the elbow and the carpometacarpal articulations). The commonest example of this function is typing or playing a piano. One might add two other basic maneuvers: that of striking or pounding with the closed fist and that of the scissors grip or holding objects between the fingers. Neither of these has much practical application as compared to the first three.

A cross section of a normal interphalangeal joint (fig. 1) demonstrates the apposing pads of hyaline cartilage separated from their epiphysial bones by the subchondral bone plate and surrounded by synovial membrane. It is the alteration of these structures brought about by the various rheumatic diseases that leads to various deformities, thereby interfering with the normal functions of the joint.

Rheumatoid Arthritis

Early rheumatoid arthritis is characterized by swelling of the proximal interphalangeal (PIP) joints of the fingers, giving the characteristic "fusiform" or "spindle-shaped" appearance (fig. 2*A*). In the case illustrated the disease had been present only two weeks when the picture was taken. An x-ray was entirely normal. At this stage the synovial membrane showed only mild inflammatory changes with proliferation of the lining cells, capillary congestion, and edema (fig. 2*B*).

As rheumatoid arthritis continues it may take any number of forms. Figure 2*C* shows the hands of a woman who had had active rheumatoid arthritis for over 10 years. During that period there had been numerous acute inflammatory episodes involving various interphalangeal joints. On the whole, however, the arthritis had remained controlled by an active therapeutic regimen including gold intramuscularly, hydrocortisone intra-articularly, steroids orally, and physical therapy. The distal interphalangeal (DIP) joints of the little fingers were involved after about the second year of the disease and, as the photograph shows, were the only ones to manifest residual damage. The x-ray (fig. 2*D*) shows the flexion deformities of these two joints and, in addition, narrowing of the joint space indicative of cartilaginous destruction of numerous interphalangeal joints at the proximal and distal level as well as at the metacarpophalangeal articulation in the index fingers. The synovial membrane

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in this case showed rather marked hypertrophic villi infiltrated with many lymphocytes and plasma cells.

Many cases of rheumatoid arthritis will remain arrested at this stage, but others will progress to further deformities. Most characteristic is the prominent ulnar deviation with flexion contractures of the fingers illustrated in figure 2*E* and *F*. This is brought about by muscular pull of interossei and flexor muscles after damage to the metacarpophalangeal joints. In this case the right index finger showed imperfect extension, due to damage with probable fraying of the extensor tendons. As noted in the x-ray (fig. 2*E*), there has been narrowing of many of these joints with some destruction. It will be seen here that ulnar deviation is minimal, indicating that it had been overcome manually by holding the fingers in the correct position to obtain the x-ray. The synovial membrane in this case showed evidence of chronic involvement with thickening of the lining cells, scarring of the subintimal layer, and marked round cell infiltration of the entire membrane. As noted in the next case (fig. 2*G*), normal alignment of the fingers can be maintained, even in a case of over 10 years' duration. Here ulnar deviation is not seen, having been prevented by proper physical therapeutic measures.

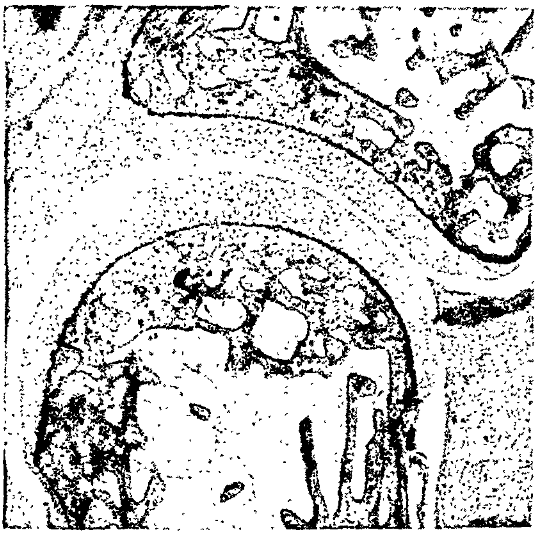

Fig. 1.—*Cross section of normal interphalangeal joint.*

Extreme cases of rheumatoid arthritis may progress to complete ankylosis (fig. 2*H*), with the x-ray showing complete loss of joint structures (fig. 2*I*). But some of the severe cases of rheumatoid arthritis show an absence of the ankylosing characteristic. Instead, there is resorption of the epiphysial bone (fig. 2*J*). The muscle pull shortens the finger, throwing the skin into folds (fig. 2*K*). If one grasps the distal phalanx the hand can then be extended to its original length, giving the name of "opera-glass hand."

Other Diseases

Osteoarthritis affecting the hand is seldom as disabling as rheumatoid arthritis. For this reason it is frequently neglected from the medical standpoint. Nevertheless, at times it can be extremely painful, and in persons who use their hands continuously, such as typists and pianists, it may indeed cause prominent disability.

Heberden's nodes, occurring in middle-aged women, are familiar to all. X-rays will demonstrate only slight narrowing of the distal joint spaces, with occasional slight lipping of the bone margins. A cross section of such a joint will show fairly well-preserved cartilage with early osteophyte production. At times these nodes may become acutely inflamed, presenting a picture of swelling and redness. No difference in the x-ray is seen unless there has been further progression of the condition with additional destruction of cartilage and further narrowing of the joint space. As the condition continues the pathological specimen will show erosion, fibrillation, and fraying of the cartilage. At times the nodes may grow to tremendous size, in which case the x-ray will show not only narrowing of the cartilage but cystic degeneration in the subchondral bone. Such a node is illustrated in figure 3*A*.

Certain cases of rheumatoid arthritis are accompanied by psoriasis. If exacerbations and remissions of the two conditions coincide and the distal interphalangeal joints are involved and resorption of bone takes place, the criteria have been met for a diagnosis of "psoriatic arthritis." In the early stages the arthritis will resemble classic rheumatoid arthritis, but as time goes on there is usually severe deformity with chronic skin discoloration (fig. 3*B*). The x-ray in such a case is strikingly similar to that previously referred to as showing "opera-glass hand."

Although less common than rheumatoid arthritis and osteoarthritis, gout may at times affect the hands, producing crippling deformities (fig. 3*C*). The x-ray (fig. 3*D*) shows marked destruction of the joint surfaces extending into the bony shafts. A typical tophus here shown in cross section (fig. 3*E*) produces the well-known "punched out area."

Scleroderma, while not actually involving the joints, may by its contracting action immobilize the hand and make it practically useless (fig. 3*F*). X-ray in such a case will show rather marked osteoporosis due to the lack of motion, but the joints themselves are found to be well preserved. Generalized calcinosis may produce similar restrictions of motion, with the x-ray (fig. 3*G*) showing small flecks of calcium throughout the extra-articular areas. Dupuytren's contracture may limit the use of one or more fingers, but here again x-rays usually demonstrate normal articular structures.

Patients afflicted with such deformities find it necessary to curtail sharply the use of their hands and to alter the basic functions as well as they can. Figure 3*H* shows a patient with far-advanced rheumatoid arthritis feeding herself.

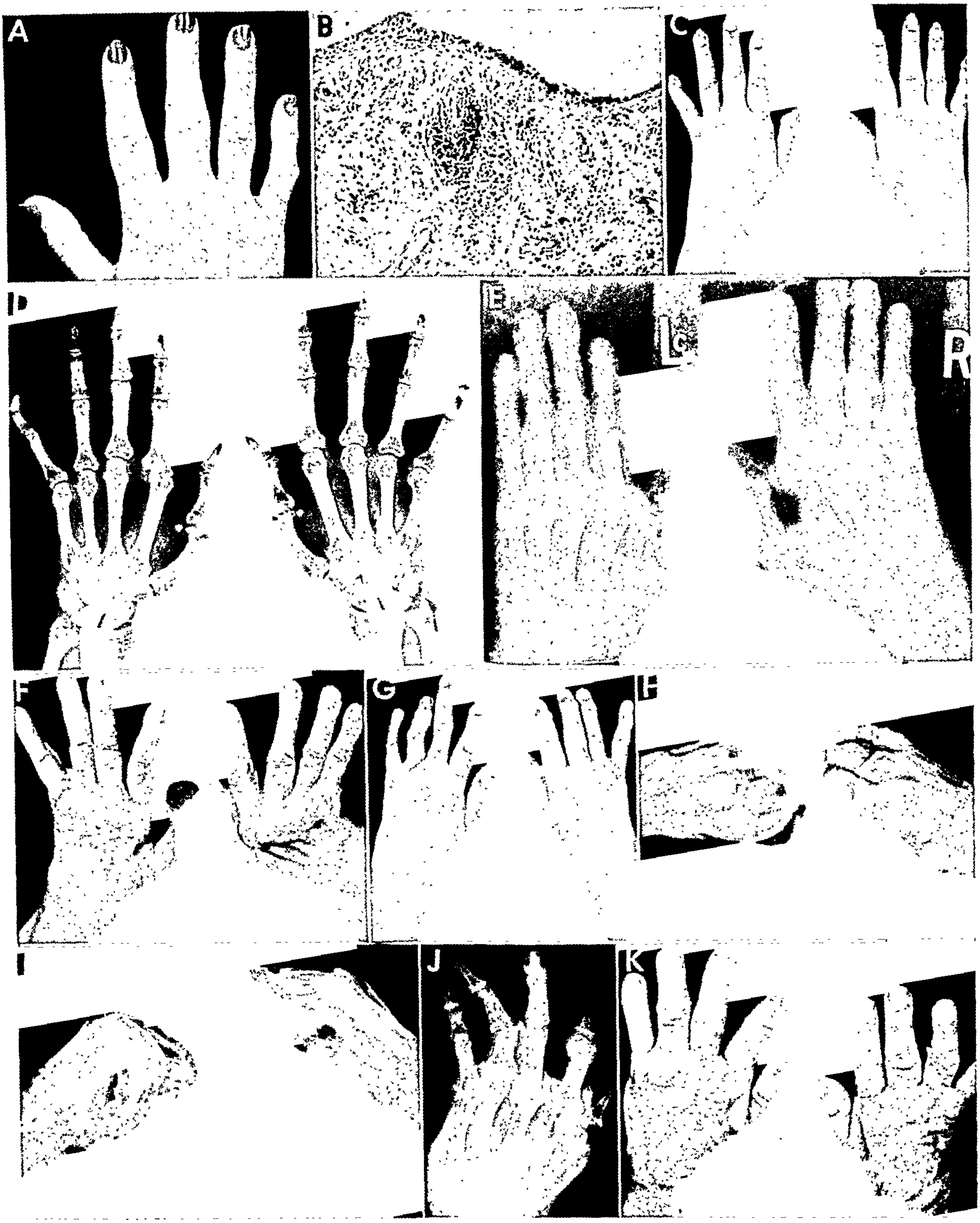

Fig. 2.—*A*, early rheumatoid arthritis, with swelling of proximal interphalangeal joints of fingers. *B*, mild inflammatory changes in synovial membrane at early stage of disease. *C*, hands of woman with active disease, controlled by therapeutic regimen, for over 10 years. *D*, flexion deformities of distal interphalangeal joints of little fingers and narrowing of joint space (same patients as in figure 2*C*). *E*, narrowing of joints with some destruction. *F*, flexion contractures of fingers (same patient as in figure 2*E*). *G*, maintenance of normal finger alignment in case of over 10 years' duration. *H*, complete ankylosis in extreme case. *I*, complete loss of joint structures (same patient as in figure 2*H*). *J*, resorption of epiphysial bone in severe case without ankylosis. *K*, shortening of fingers with muscle pull (same patient as in figure 2*J*).

Treatment

With current modes of therapy, many of the severe deformities can be avoided and disability reduced to a minimum. General measures designed to reduce the inflammatory reaction (which, although *it occurs primarily in rheumatoid arthritis,* may also at times occur in all the other conditions) are well known and usually extensively used. Particularly valuable are salicylates, phenylbutazone, and the steroids. When only a few joints show active inflammation intra-articular administration of hydrocortisone may give benefit.

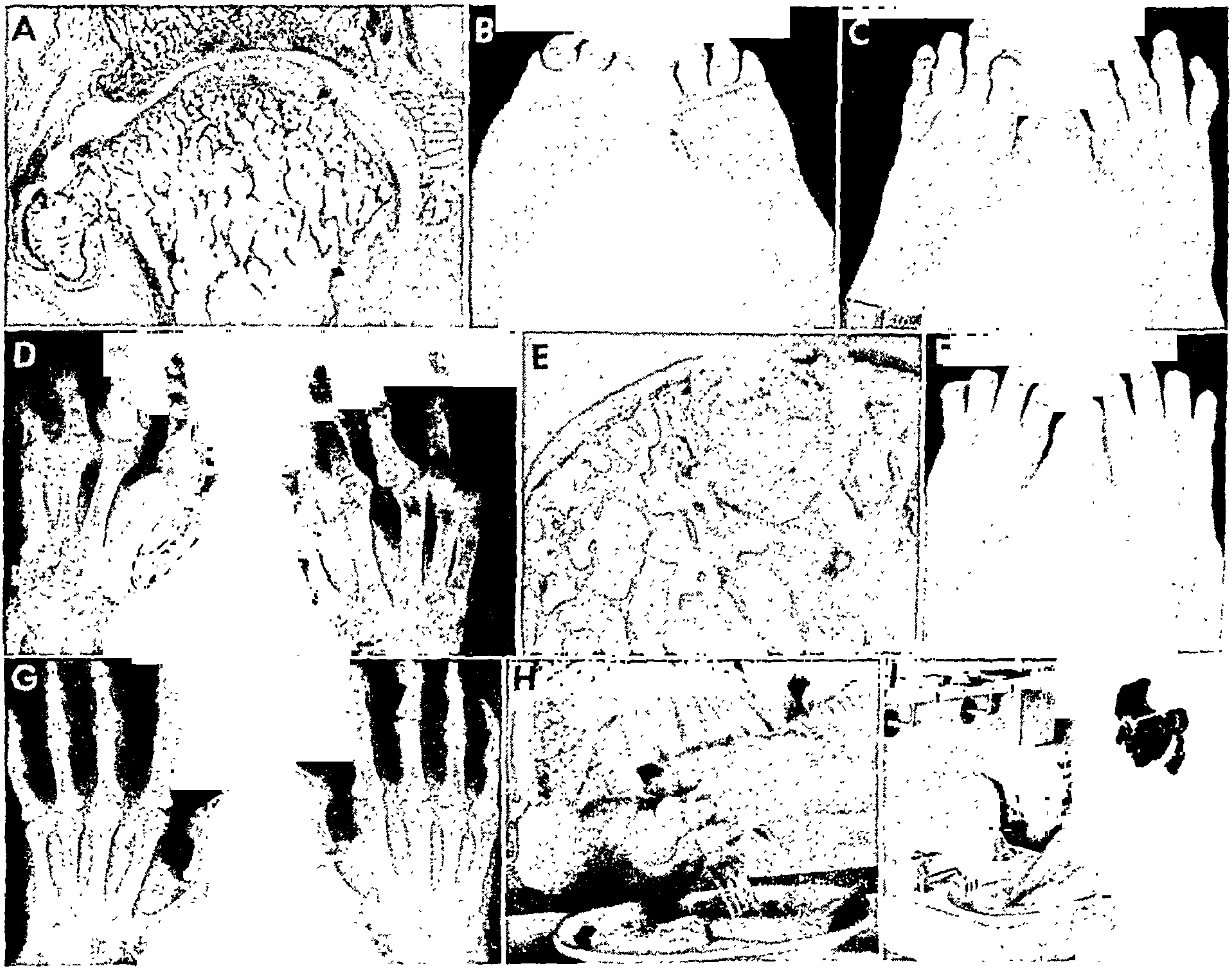

Fig. 3.—*A,* Heberden's node with cystic degeneration in subchondral bone. *B,* severe deformity in patient with rheumatoid arthritis and psoriasis. *C,* hands affected with gout. *D,* marked destruction of joint surface (same patient as in figure 3*C*). *E,* typical tophus in patient with gout. *F,* hands of patient with scleroderma. *G,* flecks of calcium throughout extra-articular areas in generalized calcinosis. *H,* patient with far-advanced rheumatoid arthritis feeding herself. *I,* home therapeutic measure.

Physical therapeutic measures familiar to the physiatrist are still too often overlooked by the prescribing physician. These include infra-red, diathermy, paraffin, whirlpool, and ultrasonic treatments.

Physiatrists today have a tendency to neglect massage, but in these rheumatic conditions it holds an extremely important place and should not be ignored. Active use of the hands on the occupational and physical therapy tables is of use in restoring partially disabled hands which have been the subject of previous neglect.

Home physical therapy—the simplest of all—may also be the most beneficial, if the patient is willing to cooperate by spending a short period once or twice a day in self-treatment. This can include simple exercises preceded by a period of infra-red radiation or exercising of the hands under hot water (fig. 3*I*).

Summary

The hands are the most important members of the body from the economic standpoint and are convenient members both for diagnosis and for treatment. Active and vigorous therapy is essential if crippling deformities are to be prevented.

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CLINICAL NOTES

GASTROUMBILICAL FISTULA DEVELOPING AFTER EXTERNAL BLUNT TRAUMA TO ABDOMEN

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and
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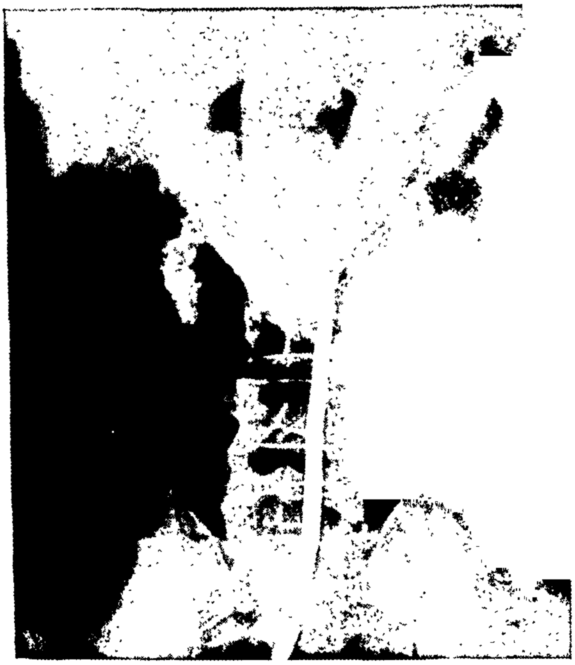
This unusual case history of a gastrocutaneous fistula developing after external blunt trauma to the abdomen in a 27-year-old male is recorded for interest. We are unable to find a similar case in the medical literature. Gastrocutaneous fistulas are rare, and most recorded cases occur after operation or penetrating wounds of the abdomen and stomach. A few cases have been recorded as developing after perforated gastric ulcers.[1]

Report of a Case

A 27-year-old male was admitted to the Los Angeles County Tuberculosis Sanatorium on Nov. 13, 1958, with moderately advanced pulmonary tuberculosis. The admission examination revealed also a draining fistula in the umbilical area, the drainage being a light tan color without any particular odor. The patient stated that about one month prior to the admission he was lifting a large sack of heavy books which were being discarded. While lifting the heavy sack, he stumbled and fell, the corner of the bottom book hitting him in the umbilical area of the abdomen. This caused immediate tearing pain in the umbilical area but no visible break in the skin. Three days later brownish-yellow drainage from the umbilical area developed.



Gastroumbilical fistula in abdomen.

It was felt on admission that this was probably either a patent vitelline duct or urachus. Roentgenograms were taken after injection into the tract of diatrizoate (Hypaque) sodium, and a gastroumbilical fistula was demonstrated as shown in the figure. This was a surprising development. The patient was again carefully questioned to be sure that he was not withholding history of a penetrating wound of some sort, such as a knife stab or ice pick wound. He was also questioned regarding swallowing of any sharp objects such as pins or fish bones. He stood by his story. There had been no other incidents of trauma to the abdomen; he had enjoyed good health until the present history; there had been no knowledge of swallowing of sharp foreign bodies which might have penetrated the gastric wall; and there was no history of abdominal or gastrointestinal pain or disturbance of any kind prior to this episode.

On Dec. 11, 1958, the fistulous tract was excised through a small epigastric incision. A 3-cm. tract extending from the most dependent part of the greater curvature of the stomach to the anterior abdominal wall at the umbilical area was encountered. Other than the fistulous tract, there were no adhesions between the stomach and the parietal wall. In the greater omentum at the site where the fistula originated from the greater curvature of the stomach, there was an area of induration which was thought to be organization of a hematoma and perhaps some fat necrosis. The tract was excised by taking a 3-cm. divot of stomach where the fistula began and by clamping and excising the tract where it ended at the anterior parietal wall. On gross examination, a small central dimple in the divot of stomach removed indicated the gastric origin of the fistula, and a probe could be inserted easily through the fistula. No gross reaction was present in the gastric mucosa. Microscopic exami-

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nation of the paraffin sections revealed a tract lined with gastric mucosa out to where it joined the skin surface. There was only minimal inflammatory reaction as indicated by scattered round cells in the submucosa. A minute granulomatous focus in the fatty omentum appeared to be a foreign-body reaction with round cells, a few giant cells, and some necrotic material.

Comment

It is difficult to explain the development of this gastrocutaneous fistula on the basis of the blunt trauma sustained. Perhaps a hematoma could have compressed and devitalized a small area of stomach which adhered to the anterior parietal wall. The trauma itself perhaps devitalized the skin in the umbilical area. The rapid development of the fistula is difficult to explain also. There is no evidence present which might incriminate peptic ulceration or developmental factors. A tuberculous involvement seems very unlikely. After careful check, we feel the details of the history are honestly reported and believe that this is a case of gastroumbilical fistula resulting from blunt external trauma.

Summary

A 27-year-old male sustained blunt trauma to the external umbilical area of the abdomen from a large bag of heavy books which fell on him. There was sudden local pain, and three days later a draining fistula developed. X-ray studies after injection of diatrizoate (Hypaque) sodium into the tract revealed a gastrocutaneous fistula. Pathological examination of the excised fistula revealed no specific cause. The 3-cm. tract was lined with gastric mucosa to the skin surface with only minimal round cell reaction and, in one area of the omentum, a foreign-body type of reaction.

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STEROID THERAPY IN SEVERE BACTERIAL ENDOCARDITIS

REPORT OF A CASE

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Alfred Vogl, M.D., New York

Experience has shown that, despite vigorous antibiotic therapy, 30% of the patients with bacterial endocarditis die from the initial infection and another 42% either die later or are left with increased disability as a result of the damage superimposed on the underlying heart disease by the infection.[1] The need for early diagnosis and prompt institution of potent therapy has, therefore, been stressed.

Fever of undetermined origin for more than a week in a person with an apparently organic heart murmur has become widely accepted as sufficient criterion for the clinical diagnosis of bacterial endocarditis and as an indication for starting therapy, without waiting for other more decisive clinical or laboratory evidence.[1] Various antibiotic regimens have been proposed for their superiority in bacteriologically obscure and resistant cases. However, no significant improvement in the above statistics has occurred since 1948, and the need for new methods of management is evident.

The following case is reported to demonstrate the dramatic effect of vigorous steroid therapy in a critically ill patient with bacterial endocarditis whose condition had been deteriorating rapidly despite treatment with large doses of antibiotics.

History

The patient was a 53-year-old man who gave a history of bronchial asthma since childhood, with frequent episodes of wheezing which had become constant and associated with exertional dyspnea during the past 8 to 10 years. The patient also reported an episode of acute rheumatic fever at the age of 32, when he was hospitalized for nine months and told that he had a heart murmur. During the previous six months dyspnea on exertion had increased and greatly impaired his capacity for work.

He consulted one of us (B.P.L.) on Feb. 1, 1958, two weeks prior to the present illness. He appeared dyspneic, with a respiratory rate of 30 per minute. His oral temperature was 99 F (37.2 C). The chest showed an increase of the anteroposterior diameter, widening of the intercostal spaces, and moderate hyperresonance. Diffuse wheezing, predominantly

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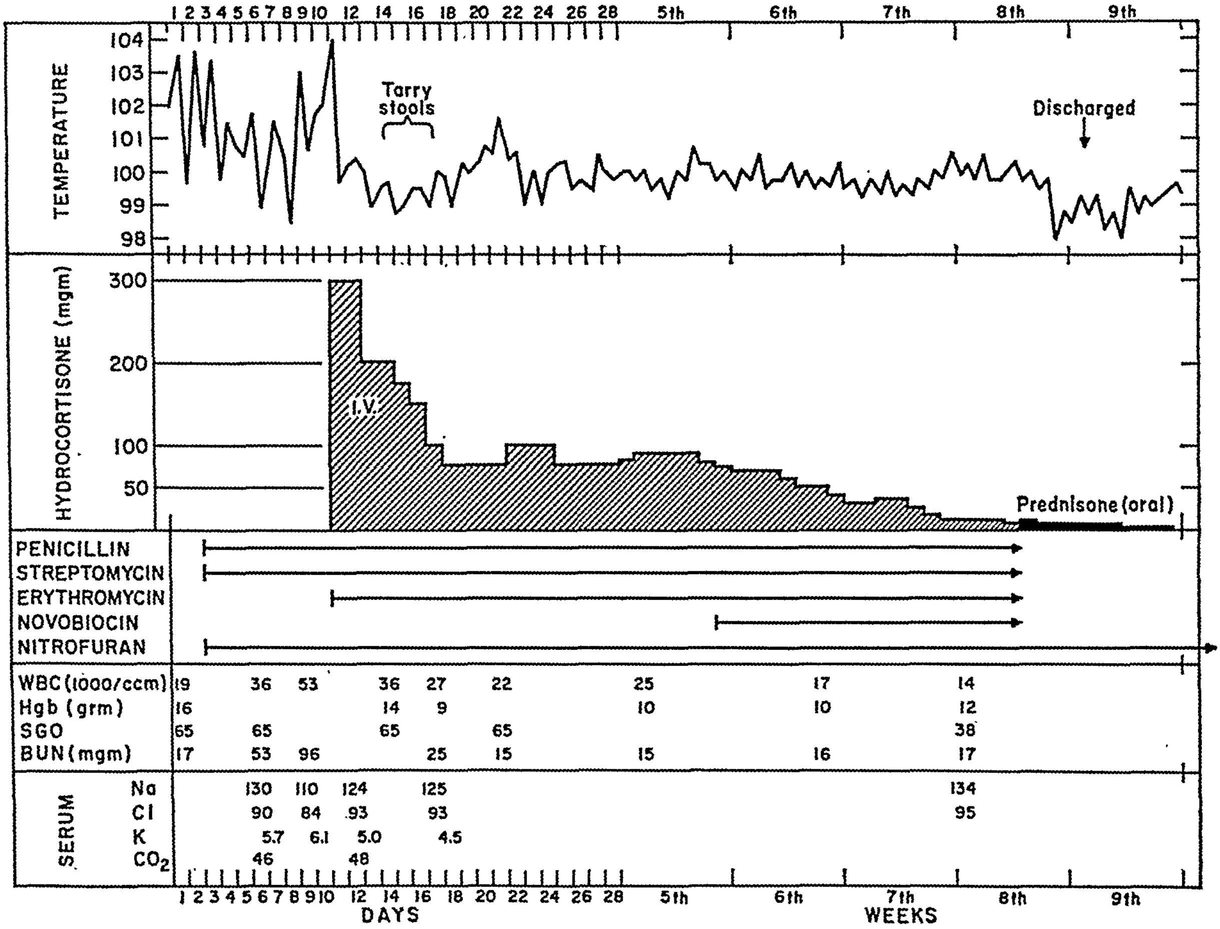
expiratory, and coarse rhonchi were heard over the lungs, along with intensification and prolongation of the expiratory phase. Medium to coarse moist rales were noted at the posterior bases. The heart was enlarged, with the point of maximal impulse in the sixth intercostal space near the anterior axillary line. The ventricular rate was equal to the pulse rate at 88 per minute. The pulmonic second sound was accentuated. The other heart sounds were almost inaudible in the presence of loud murmurs of aortic stenosis and insufficiency and mitral insufficiency. The blood pressure was 180/60 mm. Hg. The liver edge was not felt, but there was fulness in the right upper quadrant extending to 2 fingerbreadths below the costal margin. The spleen was not palpable. Edema was not present. The hemoglobin level was 13.1 Gm. per 100 ml. The white blood cell count was 10,500 per cubic millimeter with a normal differential. The erythrocyte sedimentation rate was 31 mm. per hour (Westergren). The urine showed a specific gravity of 1.020, a trace of protein, and a negative result on the test for reducing substance. There were 50 erythrocytes and 10 to 12 leukocytes per high-power field. The Venereal Disease Research Laboratory test gave a negative result. Fluoroscopy showed enlargement of the cardiac silhouette, especially of the left ventricle, and a widened aorta.



Course of disease in patient with bacterial endocarditis.

The diagnostic impressions at that time were listed as (1) chronic asthmatic bronchitis, probable bronchiectasis, and pulmonary emphysema; (2) rheumatic heart disease, inactive, with enlarged heart, aortic stenosis and insufficiency, mitral insufficiency, regular sinus rhythm, and possibly early congestive heart failure; and (3) chronic glomerulonephritis. The patient was advised to maintain a regimen of bronchodilator medication. A course of tetracycline therapy was ordered for the chronic pulmonary infection but was not carried out by the patient.

Course of Disease

The patient was next seen at his home 12 days later for complaints of severe chest pain, chills, and fever of three days' duration. The chest pain had begun as a substernal oppression which lasted overnight and, on the following day, changed to a sharp pleuritic pain in the left side. The patient appeared to have acute toxemia, with a rectal temperature of 102 F (38.9 C). The pulse was regular with a rate of 90 per minute and occasional dropped beats, and the blood pressure was 165/60 mm. Hg. Increased moist rales were noted at the lung bases posteriorly and laterally, more on the left than on the right. Findings were otherwise as noted on the previous examination. The electrocardiogram showed Wenckebach periods with P-R intervals ranging from 0.17 to 0.21 seconds, an atrial rate of 100, and a ventricular rate of 90 per minute. The QRS and Q-T intervals were 0.08 and 0.36 seconds respectively. The P wave in lead 3 was notched and in aVL diphasic. The T wave in leads 1, 2, and V_6 was inverted, in V_5 diphasic, in aVR upright, in 3 low, and in aVF isoelectric. There was a QS wave in lead 3 and a Q wave in aVF.

Our first impression was that the patient had suffered an acute myocardial infarction, possibly complicated by pulmonary embolization, and an exacerbation of his chronic bronchitis with bronchopneumonia. Because of the toxic appearance and the electrocardiographic changes, the possibilities of acute endocarditis and/or myocarditis were also considered. The patient was admitted to the Madison Avenue Hospital, New York, the next morning, and a regimen of strict bed rest, digitalization, and anticoagulant therapy was started immediately. On the next morning, after five specimens of blood had been drawn for culture, a program of antibacterial therapy, consisting of 3,600,000 units of penicillin and 1 Gm. of streptomycin per day intramuscularly and 400 mg. of nitrofurantoin orally per day, was added for treatment of the apparent pulmonary and renal infections (see figure).

On the second hospital day the patient experienced severe left lower abdominal pain and tenderness with constipation; these were interpreted as signs of either acute diverticulitis or mesenteric embolism. Some relief was obtained with upper colonic irrigation. The course during the following days was characterized by fever with temperatures of 99.8 to 101.6 F (37.6 to 38.6 C) as well as by dyspnea at rest, chest pain, abdominal pain and distention, constipation, and episodes of confusion and delirium.

On the sixth hospital day the patient repeatedly coughed up small amounts of dark clotted and bright red blood and suffered short episodes of pulmonary edema. The systolic murmurs heard over the aortic and apical areas became much louder, and the diastolic pressure dropped to zero while the systolic remained at 160 mm. Hg. This combination of events and findings suggested perforation or rupture of an aortic cusp and was regarded as additional strong evidence of bacterial endocarditis. For this reason the effect of the anticoagulant therapy was rapidly reversed with intravenous administration of vitamin K_1, and the antibiotic regimen was reinforced by increasing the penicillin dosage to 40 million units daily by vein, while streptomycin and nitrofurantoin therapy was continued. Laboratory test at that time showed the hemoglobin level to be 15 Gm. per 100 ml., white blood cell count 36,000 per cubic millimeter with a moderate shift to the left, blood urea nitrogen level 53 mg. %, sodium level 130 mEq. per liter, potassium level 5.7 mEq. per liter, chloride level 90 mEq. per liter, carbon dioxide content 45 vol. %, and serum glutamic oxalacetic transaminase level 65 units. On the same evening another episode of pulmonary edema occurred. The patient showed clinical signs of shock with cold wet skin and cyanosis. He was semicomatose and appeared moribund for about three hours but eventually responded to persistent symptomatic treatment.

The course remained stormy for the next five days despite the increased dosage of antibiotics, and he had a septic fever with temperatures up to 103 F (39.4 C), recurrent bouts of pulmonary edema, signs of intestinal obstruction with increasing abdominal distention, and progressive uremia. The patient's misery was aggravated by nausea and intractable singultus, which prevented him from taking food and fluids by mouth. A Miller-Abbott tube was passed into the stomach on the eighth hospital day and began to advance two days later. On the ninth hospital day several generalized convulsions occurred. The patient was confused or stuporous most of the time, and he appeared extremely weak and severely cyanotic. Respirations were shallow, labored, and rapid. The lungs showed wheezing throughout, and crackling rales at the lower two-thirds of both lungs posteriorly and at the bases anteriorly. The loud heart murmurs persisted. Bowel sounds were sparse, with occasional peristaltic rushes. Urinary output remained commensurate with the total fluid intake, which approximated 1.5 liters daily.

Laboratory studies on the ninth hospital day revealed a leukemoid blood picture, with a leukocyte count of 53,000 per cubic millimeter and a marked shift to the left, and azotemia with a blood urea nitrogen level of 96 mg. %. Electrolyte levels were as follows: sodium 110 mEq. per liter, chloride 84 mEq. per liter, potassium 6.1 mEq. per liter, calcium 9.5 mg. %, and carbon dioxide–combining power 46 vol. %. The hemoglobin level was 14 Gm. %, and the serum glutamic oxalacetic transaminase level was again 65 units. Blood and urine cultures obtained on the first hospital day remained negative, and throat and sputum cultures grew no pathogens or predominant organisms.

An attempt was made to compensate for the severe electrolyte disturbance by the intravenous administration of 1 Gm. of sodium chloride per 24 hours from the 9th through the 14th days. Calcium gluconate was added to the infusion. After the first day of electrolyte replacement a slight gain in strength was noted. There was a brief improvement in the patient's alertness, but after about 12 hours he again became confused. No further attacks of pulmonary edema occurred during the six days of salt administration. The over-all picture, however, continued to appear desperate, with rising temperature, persistent congestive heart failure, cyanosis, prostration, and striking wasting of subcutaneous and muscular tissue.

Steroid Medication

On the 11th hospital day the temperature rose to 104 F and the patient again appeared about to die from overwhelming toxemia. For this reason, we decided to try a vigorous course of steroid medication. At 3 p.m. on that day, 100 mg. of hydrocortisone was given as a single intravenous injection, 100 mg. was added to the infusion of 5% dextrose solution and 20 million units of penicillin in water which was being given at the time, and another 100 mg. was added to the next infusion of that 24-hour period. At the same time 1.5 Gm. of erythromycin was added to the daily intravenous regimen. By midnight of the same day, the temperature had dropped from 104 F to 99.8 F. It remained approximately at that level throughout the subsequent hospital course. The drop in temperature was associated with a striking improvement in the patient's symptoms, general appearance, and physical findings. Convulsions ceased, cyanosis faded, and the intensity of the heart murmurs decreased gradually. The congestive failure was easier to manage from that point on. The mental status improved markedly, and the patient developed a voracious appetite. Laboratory studies performed on the 12th hospital day showed an improvement in the electrolyte status as compared with the values obtained three days earlier. The blood urea nitrogen level was 63 mg. %, sodium level 124 mEq. per liter, chloride level 93 mEq. per liter, potassium level 5.0 mEq. per liter, and carbon dioxide–combining power 48 vol. %.

The persistence of a most severe infection and/or stress despite the obvious clinical improvement was, however, revealed by a leukocyte count of 43,000 per cubic millimeter with a marked shift to the left. The high serum glutamic oxalacetic transaminase value (65 units) still present at that time suggested continued tissue destruction, probably of the kidney, because of the persistent proteinuria, microscopic hematuria, and pyuria, and/or of the myocardium, as suggested by the clinical picture.

Gastrointestinal bleeding occurred during the third, fourth, and fifth days of steroid administration, with the appearance of several large tarry stools and a drop in hemoglobin level from 14.0 to 9.0 Gm. %. The intravenous dosage of hydrocortisone was decreased from 200 mg. per day to 70 mg. per day during the four days after the onset of melena, and the patient received frequent doses of Gelusil (magnesium trisilicate and aluminum hydroxide) and milk of magnesia. Fortunately, the melena stopped and no further drop in the hemoglobin level occurred. By that time, the Miller-Abbott tube, having been in place for nine days, had advanced to its full length and abdominal distention and other symptoms of intestinal obstruction had subsided. The tube was therefore removed.

On the 22nd hospital day, the temperature rose again to 101.6 F and laboratory data indicated the persistence of systemic infection. The intravenous dosage of hydrocortisone was therefore again increased to 100 mg. daily and 3 Gm. of novobiocin per day intramuscularly was added to the antibiotic therapy. From that point on, uninterrupted improvement took place. The antibiotic regimen was continued, the intravenous dosage of hydrocortisone was gradually tapered off during the next five weeks, and the congestive heart failure was treated with gitalin and frequent mercurial injections. Bouts of incipient pulmonary edema still occurred but could be controlled by conventional means without difficulty. The blood urea nitrogen level returned to normal after the third hospital week, and electrolyte levels also remained within normal limits. However, proteinuria, pyuria, and a leukocyte count above 20,000 per cubic millimeter persisted up to the seventh hospital week. The hemoglobin level rose from 9.0 to 12.0 Gm. % after treatment with colloidal iron given intramuscularly. Small oral doses of prednisone were substituted for intravenous administration of hydrocortisone on the 53rd hospital day, at which time all antibacterial therapy was discontinued except for that with nitrofurantoin, which was given for another month. Prednisone dosage was tapered off daily from an initial dose of 7.5 mg. on the 53rd hospital day until it was discontinued one week later, after which the patient received no further steroid therapy.

Follow-up Findings

The patient was discharged on the 57th hospital day. At the time of discharge he felt well except for moderate dyspnea and marked weakness. There was still slight wheezing in all lung fields and moist rales at both posterior bases. The liver edge was 2½ fingerbreadths below the costal margin. Tremendous weight loss was evident. No edema was present. Noteworthy was a rise of the diastolic blood pressure from 0 to 30 mm. Hg during the last (eighth) hospital week. The serum glutamic oxalacetic transaminase level fell into the normal range for the first time, but the erythrocyte sedimentation rate was still 36 mm. per hour (Westergren). Urinalyses performed during the last week showed proteinuria (0 to trace), occasional leukocytes, and a rare red blood cell on one occasion. Blood, throat, and urine cultures showed no significant growth after being held for eight weeks.

During the five months after discharge up to the time of this writing, the patient has remained afebrile and asymptomatic except for generalized weakness and easy fatigability. Therapy has included nitrofurantoin, 200 mg. daily by mouth for the first month at home, and gitalin, 0.5 mg. daily, in conjunction with a low-salt diet. Symptoms and signs of congestive heart failure have not recurred, and the lung fields have been clear except for a moderately prolonged expiratory phase and scattered wheezes. Examination on June 10, 1958, showed an oral temperature of 98 F (36.6 C), a regular pulse rate of 76 per minute, respirations 20 per minute, and blood pressure 160/30 mm. Hg. The liver was palpable 1 cm. below the costal margin. The urine showed traces of protein and 0 to 3 leukocytes per high-power field. The hemoglobin level was 16.7 Gm. % (Sahli), microhematocrit value 47%, and white blood cell count 8,000 per cubic millimeter with a normal differential. When presented at the hospital staff conference, he looked and felt well and specifically denied all symptoms of congestive heart failure on questioning. Recently he has been able to perform his usual work for short periods of time.

In summary, this was a case of bacterial endocarditis of undetermined type, superimposed on rheumatic heart disease chiefly involving the aortic valve. The course was complicated by pulmonary embolization, intestinal obstruction (possibly due to mesenteric embolism), probable perforation of an aortic cusp, severe congestive heart failure, uremia, hyponatremia, hypochloremia, hyperkalemia, and chronic asthmatic bronchitis. The fulminating course with high temperatures and progressive toxemia was dramatically aborted by the intravenous administration of hydrocortisone. During steroid therapy the course was further complicated by a three-day episode of massive gastrointestinal hemorrhage. The infection ultimately responded to a regimen which included several antibiotics in high dosage. On clinical healing of the bacterial endocarditis, the diastolic blood pressure rose from 0 to 30 mm. Hg.

Factors Limiting Effectiveness of Therapy

Analyses of large numbers of cases of bacterial endocarditis have shown that various factors limit the effectiveness of therapy in any given case with some degree of predictability.[2] Such factors as severe preexisting valvular deformity, the presence of congestive heart failure at the onset of the infection, and involvement of the aortic valve have been found to influence the ultimate prognosis adversely. Involvement of vital organs by metastatic abscess formation also increases the number of disabling sequelae and the mortality, even if bacterial cure can be accomplished. Prolonged duration of infection before institution of treatment is generally believed to alter the prognosis unfavorably, but, obviously, this impression is difficult to prove statistically. The nature of the infecting organism and its sensitivity to antibiotics are critical factors in determining the possibility of bacterial cure. For example, in patients infected with penicillin-sensitive organisms, bacterial cures are reported obtained in from 80 to 90%, whereas staphylococcic infections show an over-all cure rate between 40 and 50%.[2]

The importance of the infecting organism is overshadowed, however, by the "host-parasite relationship" which becomes established in the course of this disease. It is this phenomenon which actually distinguishes bacterial endocarditis from many other bacterial infections, since in this particular infection the host responds with a compromise between a granulomatous and pyogenic reaction. Apparently, the reaction established in a given case determines the clinical picture and alters such factors as toxicity and length of course. As with most granulomatous processes the host defense slows the progress of the infection. At the same time it permits and actually causes, to a certain extent, the relentless destruction of tissue while providing protection for the invaders. These factors have attained clinical importance since the advent of potent antibacterial agents because the sealing up of masses of organisms in vegetations reduces their availability in the blood stream for diagnosis and decreases their exposure to the therapeutic agents.

The question as to which antibiotic treatment is the most effective remains a matter of controversy. Hunter,[3] Friedberg,[1b] and Newman and co-workers [1a] hold that bacteriostatic agents offer little or no hope for permanent bacterial cure. Finland [1d] and Kellow and Dowling,[4] on the other hand, depend on in vitro sensitivity studies for the selection of an antibiotic regimen and use bacteriostatic agents when indicated by these studies. Both schools recommend antibiotics in combination, but the former uses penicillin and streptomycin almost exclusively, taking advantage of the virtually unlimited dosage of penicillin which can be administered to overcome bacterial resistance demonstrated in the laboratory and/or clinically. Interestingly, both schools report difficulties with similar types of conditions (e.g., staphylococcic infections and culture-negative cases) and almost identical total bacterial cure rates.

The fact that cure of infection is only one of the major problems in the management of this disease is demonstrated by a study of 52 cases reported from the Bronx Veterans Administration Hospital by Newman and associates.[1a] In this series, an overall bacterial cure rate of 69% was observed. Of these patients, however, one-third died of congestive heart failure within a short period, one-third suffered increased disability attributable to damage produced by the infection, and only one-third returned to an asymptomatic state.

Use of Steroids

Considering these data along with the fact that the prognosis of the disease has not improved significantly since 1948 despite the availability of several new antibiotics, it becomes evident that other phases of the disease must be attacked while destruction of the invaders is effectively pursued. The host-parasite relationship would appear to be a proper target for such an attack, in view of its fundamental importance in the pathogenesis of this disease. However, to our knowledge, no systematic attempts have been made to alter the local tissue response to the infection. Anticoagulants were tried with a view to decreasing fibrin clot formation in the vegetations but were soon withdrawn because of the frequent occurrence of hemorrhagic complications.[5] Steroids are, to our knowledge, not considered in the American literature in this connection, except for their use in the management of an incidental penicillin allergy[6] and, in one recent article,[1d] are actually rejected as being useless and hazardous in this disease.

However, increasing data are accumulating which demonstrate the beneficial action of steroids in overwhelming acute infections, as well as in chronic granulomatous processes, such as tuberculosis, brucellosis, and typhoid.[7] Most of these reports indicate that steroid therapy can be extremely effective in reversing severe acute and chronic intractable toxic states which threaten to kill the patient before antibacterial therapy can change the clinical course. In our case, it was hoped that steroids could temporarily suspend the life-threatening systemic toxicity and, at the same time, possibly alter the unfavorable tissue inflammatory phase of the process. Rheumatic activity which apparently occurs frequently during bacterial endocarditis[7A] would also be suppressed.

The actual mechanisms responsible for the effect of steroids in infectious disease have not been identified, but the work of Thomas[8] provides experimental evidence supporting the view that the reactivity of the reticuloendothelial system is distinctly altered and at least partially blocked by cortisone. This suppression of certain phases of the host response actually favors the propagation of the invading parasite and is undoubtedly responsible for the unfortunate infectious complications which remain a constant hazard attending the clinical use of the corticosteroids. This hazard became evident early in the steroid era and created such an impression throughout the medical world that, until recently, the presence of infectious disease was considered a strict contraindication to steroid therapy. The caution evoked by the early experience readily explains why steroids have not been used in the treatment of bacterial endocarditis up to the time of this writing. However, various other infectious diseases have recently been treated successfully with combined antibiotic and steroid therapy,[7] suggesting the need for a revision of the attitude which has prevailed toward this problem. We feel that the result observed in our case justifies further investigation of the efficacy of steroids as an adjunct to antibiotic therapy in cases of intractable bacterial endocarditis. Obviously, steroids are not indicated in the average case. In the exceptional case for which they appear indicated, however, they must be used in adequate doses for a limited period and under close observation for the possible serious complications of steroid therapy.

Summary and Conclusions

An attempt to meet the problem of overwhelming toxemia in a patient with bacterial endocarditis by treatment with high doses of intravenously given hydrocortisone has apparently been successful. The treatment of bacterial endocarditis with antibiotics attacks only one phase of this complex disease process, as demonstrated by the still unfavorable prognosis in the majority of cases.

The septic phase of the disease may be controlled and the efficacy of antibiotic therapy may be enhanced in refractory cases by the simultaneous administration of adequate steroid therapy. Steroids probably operate by inhibiting the response of the host tissues to the infecting organism, thus limiting tissue destruction and exposing the invaders more freely to antibacterial agents. In addition, reactions of systemic toxicity endangering the life of the host and rheumatic activity (if present) are suppressed. The serious nature and grave outlook of bacterial endocarditis appears to warrant further investigation of the use of steroids in severely toxemic and unresponsive cases.

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EIGHTH NERVE DEAFNESS AFTER ADMINISTRATION OF KANAMYCIN

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That the administration of kanamycin sometimes leads to eighth nerve deafness has been established by the early observations of Bunn and associates.[1] Four cases of deafness occurred after the administration of 31, 52, 80, and 84 Gm., respectively, and led the authors to conclude that "kanamycin is essentially nontoxic when given in 1.5-to-2-Gm. daily doses for less than a total of 40 Gm. In doses exceeding 40 Gm. there is a clear chance that it will produce permanent eighth cranial nerve damage and that deafness may ensue." In the same symposium, Winfield and co-workers[2] reported auditory loss in 10 of 20 patients, all of whom had concurrent renal damage. Donomae, reporting for the Committee of Chemotherapy for Tuberculosis of Japan,[3] expressed the opinion that impairment of hearing is extremely improbable if the dosage is maintained below 6 Gm. per week. White and Knight[4] reported severe deafness occurring 11 days after therapy with 2 Gm. a day of kanamycin plus 1 Gm. a day of streptomycin in a patient who had received nearly continuous treatment with streptomycin for two months previously. The most detailed report of kanamycin toxicity from the auditory nerve is that of Finegold and associates.[5] They discovered that larger total doses and total daily doses were more conducive to eighth nerve damage than were smaller doses, although one of their patients suffered partial deafness after only 13 Gm. of the drug. In the case reported here, permanent deafness followed the administration of 13 Gm. of kanamycin to a 52-year-old diabetic.

Report of a Case

A 52-year-old man, a diabetic for 25 years, had experienced a relentless series of vascular complications during the past 10 years, resulting in coronary heart disease, blindness, and gangrene. He underwent bilateral amputation above the knees and for the past three years had maintained a fairly comfortable existence. In July, 1958, he developed persistent draining furuncles with abscess formation over the left temporoparietal area and over the left arm. Staphylococcus albus was cultured from the wounds. No response was obtained from use of sulfisoxazole (Gantrisin), chloramphenicol, tetracycline, erythromycin, or penicillin.

Because his general condition worsened in August, 1958, therapy with kanamycin, 2 Gm. given intramuscularly in divided doses, was started. The blood urea nitrogen level was 27 mg.%. Four days after the kanamycin administration, difficulty in hearing was noted; voices sounded muffled and distant to him. The ringing of the telephone and the barking of a dog were inaudible, and extreme dizziness and tinnitus ensued. For 48 hours thereafter the excretion of urine became scanty; the blood urea nitrogen level rose to 64 mg.%. Believing that kanamycin was affecting the eighth nerve, we discontinued use of the drug immediately, after a total of 13 Gm. had been administered. Within the following week, bilateral deafness developed. An otolaryngologic consultant found inactive vestibular mechanisms on both sides after calorie stimulation. The hearing test revealed an average of 95% hearing loss in the patient's left ear and complete loss in the right. Several months have elapsed since the discontinuance of kanamycin therapy, with no apparent improvement in hearing. Vertigo has continued and is constant.

Comment

Kanamycin, like neomycin and streptomycin, damages the vestibular portion of the eighth nerve in certain patients. It seems probable that this effect is more likely to occur in those patients whose kidneys fail to eliminate the drug as rapidly as do normal kidneys. Under such circumstances small doses may rapidly produce toxic effects which might not occur if renal function were intact. In our opinion, kanamycin should not be given to patients with any degree of renal impairment unless it is needed as a lifesaving measure when no other microbial drug will suffice.

Summary

Permanent and almost complete eighth nerve deafness followed the administration of 13 Gm. of kanamycin in one week to a 52-year-old diabetic whose blood urea nitrogen level rose during the administration of the antibiotic.

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SPECIAL ARTICLE

This is the second of three papers presented at the Midyear Conference of the American Hospital Association, Chicago, Feb. 4, 1959. The first was published in the June 6 issue of The Journal, *and the third will appear in the June 20 issue.*

STATE JOINT MEDICOLEGAL COMMITTEES

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Dr. Sadusk has already reported on the history and the activities of the A. M. A.-A. H. A. joint medicolegal committee (The Journal, June 6). That committee can only act as a sparkplug, for the basic work must be done at the state level through the activities of a joint committee created by the state medical society and the state hospital association.

Purpose

The underlying purpose of the joint committee must be to improve patient care in the hospital setting through improved treatment methods, management technique, and basic safety across the entire spectrum of care, from the highly trained specialist on the one hand to the maids and porters on the other.

It should be pointed out that the statement of purpose is set forth in the positive and is directed toward improved patient care. There is no mention of claims prevention or holding down suits or judgments, because these are essentially negative approaches to the basic problem of doctor and hospital liability. A positive approach puts doctor and hospital liability insurance in the proper perspective. The proper function of insurance is to furnish an effective means of sharing the cost of losses that have occurred after the doctor-hospital team has done its best to properly care for the patient. In other words, insurance covers those human or mechanical errors that inevitably occur in our society, in this case in connection with patients.

The acceptance of the fact that errors are inevitable leads to the acceptance of the principle that we have a duty to reduce them to the irreducible minimum. Payment of money as compensation is a poor substitute for good health, but at least it partially fulfills the legal or moral obligation to the person who has been unnecessarily injured. This only emphasizes the fact that accident prevention not only is good business but is a basic obligation of every doctor and every member of the hospital family. The state joint committees must therefore be patient-oriented.

Functions

To carry out the basic purpose, the state joint committee shall perform the following nine functions:

1. Act as liaison between the A. M. A.-A. H. A. Joint Committee and the individual hospitals within the state. In this connection the state committee is the cornerstone of the program. On the one hand, it distributes and interprets material developed by the A. M. A.-A. H. A. committee to the individual hospitals; on the other hand, it passes on to the national committee problems, experience, and ideas uncovered or developed at the state or local level so that all hospitals and doctors can benefit from the experience of individual hospitals.

2. Act as liaison between the state medical society and the state hospital association on matters relating to professional care and professional liability problems. Experience has shown that the medical profession, if properly approached, can offer many constructive ideas on problems affecting hospitals and vice versa. Often it is not possible to tackle these on an individual hospital basis.

Among the many problems that can best be worked out by joint action at a state level are those such as (*a*) sponge counts (should a fourth count be taken at skin closing as a routine procedure?), (*b*) blood identification (can a uniform procedure be developed to assure proper identification of blood?), (*c*) surgical check lists (should the hospitals in the state uniformly use surgery check lists?), and (*d*) patient identification (who shall be responsible in surgery for final identification of the patient, the procedure to be performed, and the member on which it is to be performed?).

3. Encourage individual hospitals to establish medicolegal education committees. Dr. Groeschel in his paper will discuss the organization and functioning of such individual hospital committees; but unless their formation and continuance is given official sponsorship and active encouragement from the state level, they will neither germinate nor continue to bloom. In many states, county medical societies and area hospital councils will furnish effective assistance in this project.

Legal Counsel, California Hospital Association, and hospital member, Joint American Medical Association–American Hospital Association Committee on Professional Liability.

4. Develop a comprehensive incident reporting system as a basic tool for both the local hospital and the state committee in order to keep abreast of the changing pattern of problems relating to patient care. The A. H. A. has recently adopted a recommended form for this purpose. This form or a similar one should be approved for statewide use. Each hospital should be encouraged to share its experience with the others through some central reporting system adapted to local conditions. Patterns that would not show up in the experience of any one hospital will become evident through combining the reports of many hospitals.

5. Review incident trends and make basic recommendations for improvements. It does no good to compile statistics if they are not properly utilized.

An example of the effective use of incident reporting and analysis arose out of the California Hospital Association's experience in reviewing incidents relating to staphylococcic infections. This occurred before the rest of the country realized the nature of the problem.

As the incident trend on infections showed a continued and rapid increase, it was evident that a major problem was developing. Furthermore, although few individual hospitals had been hard hit, there was substantial evidence that the problem was widespread and required immediate action. The state hospital association contacted the state department of public health and a series of meetings was held to review the statistics and prepare remedial measures. These meetings included representatives of both medicine and nursing. A course of action was approved, and a team was sent out into the field under joint sponsorship to sell the prevention program. Those who were not aware of the problem were brought up to date, and all were instructed in the techniques of setting up individual hospital programs of prevention. The fact that the program had the joint sponsorship of the medical society and the hospital association gave it authority and acceptance that would not otherwise have been possible.

Other problems that would be subject to a similar approach would be medication errors and blood transfusion errors. Due to the rapid increase in the number of different drugs being administered as well as the apparent similarity of names, the number of medication errors is rapidly increasing. The continued confusion over the metric and the apothecary systems of drug dosage is also an unresolved problem. Hospitals are also experiencing an increasing incidence of transfusion errors due to the accelerated use of whole blood and blood products. These problems are difficult, but a careful analysis of the causation of a large number of incidents by a joint committee should eventually lead to a practical solution for better patient care.

6. Anticipate problems that will be created by the rapid progress in hospital care and techniques. This might be called the "crystal ball" technique, but actually it must be based on a rational scientific approach.

For example, a new problem that is now facing both hospitals and organized medicine is the matter of cardiac arrest. From the medical point of view, there are the following questions: When should an attempt be made to massage the heart? (Obviously, it is not indicated in all cases.) Should additional special training be provided to all surgeons? What special equipment should routinely be made available in surgery and the emergency room? Should a physician be present during the performance of dental procedures by a dentist in the hospital? These are only a few of the problems that must be faced concerning this complex subject. Both doctors and hospitals are going to be sued many times unless some sound uniform practice is developed and explained to the public, since this matter inevitably gets newspaper and magazine coverage.

7. Develop and distribute basic information and statistics within the state that will assist the individual hospital medicolegal education committee. In this connection the state committee will develop program materials and training aids as well as encourage the presentation of educational institutes on a statewide or area basis.

This is basically the problem of communication. The state committee should not preempt the activities of other established resources for this purpose but should actively utilize existing organizations and communications mediums wherever possible.

8. Coordinate the activities of the leading professional liability carriers in the state. In nearly every state there may be from 10 to 50 different insurance carriers writing professional liability insurance for doctors, hospitals, or both. By and large, the bulk of the business will be concentrated in not more than five carriers. Generally, these carriers are more concerned with their own individual problems than with the welfare of the medical profession and the hospitals. Much can be done to improve their procedures for processing claims and settlements that will be for the ultimate protection of doctors and hospitals. If the carriers realize that their methods are being reviewed and if they are given a forum in which they can review their problems with the profession and hospitals, many critical problems can be avoided. There are just as many unreasonable doctors and hospitals as there are unreasonable claims adjusters. Mutual problems and procedures can best be worked out around the conference table.

9. Develop group professional liability programs on an area or statewide basis. In my opinion, the only ultimate answer to the problem of professional liability problems is the utilization of group programs. As a matter of personal preference, I believe

there is merit in a separate program for doctors as distinguished from a hospital program. An effective program requires self-discipline, and experience indicates that the medical profession would prefer to discipline itself without any suspected interference from the side of hospital administration.

Actually, a group liability program will make the work of the state joint committee far more effective, since it will furnish in an efficient and economical manner the basic statistical material and analyses that are fundamental to the state committee.

Organization and Operation

Obviously any state joint committee should adapt itself to the pattern of organization at the state level; however, certain basic principles should be considered.

1. The committee's organization and purpose should be set forth in a written memorandum approved by the parent organizations.
2. The agreement should provide for equal representation from the state medical society and the state hospital association.
3. The committee should be appointed by and responsible to the boards of trustees of the parent bodies. This is to assure that the status of the group is unquestionable and to avoid unnecessary red tape.
4. Since this committee will be dealing with matters of fundamental importance, it should be made up of top leadership and its membership should be stable. The size is not critical, except that it should not be unduly large.
5. Arrangements should be made to adequately staff the committee. Either the hospital association or the medical society should assume this responsibility initially, with rotation an eventual possibility.
6. Regular meetings should be scheduled. There is nothing like a deadline to bring about some activity.

Comment

I assume the responsibility for the statements made in this paper, since a basic statement on the organization and purpose of the state committees has not been approved by the A. M. A.-A. H. A. Joint Committee; however, I am sure that my fellow committee members would join me in the conclusion that for the long-range good of the patient, as well as the standing and reputation of the medical profession and our hospitals, the creation and progress of joint state medicolegal committees is an absolute necessity.

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COUNCIL ON DRUGS

NEW AND NONOFFICIAL DRUGS

The following descriptions of drugs are based upon available evidence and do not in any case imply endorsement by the Council. H. D. Kautz, M.D., *Secretary.*

Cottonseed Oil Emulsion (Lipomul I.V.).—An emulsion of the refined fixed oil (cottonseed oil, U. S. P.) obtained from the seeds of cultivated plants of various varieties of Gossypium hirsutum Linné or of other species of Gossypium (Fam. Malvaceae).

Actions and Uses.—An emulsion of cottonseed oil was introduced commercially in 1958 for intravenous use in severely malnourished patients unable to take adequate amounts of food by mouth. This preparation is marketed as a 15% oil-in-water emulsion with 4% dextrose to make it isotonic. It is nonirritating to the venous epithelium. Hence, high concentrations of cottonseed oil emulsion may be infused intravenously. Because of this fact, and since fats as a class provide higher caloric yields per gram than either carbohydrate or protein, cottonseed oil is an excellent source of calories; 500 cc. of a 15% emulsion provides approximately 750 calories as contrasted to 100 calories with the same volume of 5% dextrose or 200 calories with a solution of 5% protein hydrolysate and 5% dextrose. Metabolic studies have indicated that this fat is utilized and that it retards the catabolic phase of metabolism, i. e., exerts a nitrogen-sparing effect.

From a nutritional standpoint, infusion of cottonseed oil would appear to be unexcelled as a means of highly effective parenteral alimentation. However, enthusiasm for such therapy must be tempered by the realization that the infusion of fat emulsions carries with it a definite risk of untoward reactions which range from very mild to quite severe. For this reason, cottonseed oil should be used with considerable discretion. It is not intended for routine use but should be reserved for patients with severe nutritional deficiency for whom other forms of parenteral feeding are inadequate to meet minimum caloric requirements, and it should be used only over a brief period of time. Logical candidates for such therapy might include patients with obstructive lesions or debilitating diseases who are being prepared for surgery, postoperative patients with temporarily nonfunctioning gastrointestinal tracts, patients with extensive burns, severely debilitated patients with traumatic conditions, and patients with severe nutritional depletion resulting from gastrointestinal disease. In occasional instances, intravenous therapy with cottonseed oil may be instituted as a temporary expedient in patients who are unable to absorb fat adequately from the gastrointestinal tract or in those with renal failure in whom maximum nitrogen-sparing is indicated. In all patients, the use of fat emulsions should be strictly limited to a brief period of time and should not exceed 14 infusions of 500 cc. each. The need should be sufficiently urgent to justify a small risk of dangerous reactions, and oral feeding should be resumed as soon as possible.

Untoward reactions to cottonseed oil emulsion may be either immediate or delayed. The immediate reactions generally occur early during the course of the initial or subsequent infusions. Delayed reactions, on the other hand, do not occur until after large amounts of fat have been infused intravenously.

The major type of immediate reaction, occurring in about 0.1% of patients, is characterized by back or chest pain, dyspnea, severe flushing, and urticaria. Chills, which may occur during an infusion or a few hours later, have been encountered in approximately 1% of patients. Intravenous fat infusions may also give rise to febrile reactions lasting a few hours; the incidence of these episodes (with temperatures of 100.6 F or over) has been about 3.5%. Immediate reactions of minor types include nausea, vomiting, abdominal discomfort, headache, mild flushing, dizziness, tachycardia, and elevation in blood pressure.

Delayed reactions to fat given intravenously are manifested by a symptom-complex sometimes called the "overloading syndrome." This syndrome is characterized by chills, fever, abdominal pain, nausea, vomiting, hepatomegaly, mild anemia, clotting defects, thrombocytopenia, and bleeding, particularly from the gastrointestinal tract. In patients with this syndrome, who have succumbed to their primary disease, pigmentation or fatty infiltration of the liver and/or spleen has been a frequent autopsy finding. The incidence of this type of untoward reaction is not known, although the likelihood of its development apparently increases as the number of intravenous infusions of fat increases. In most cases reported to date, symptoms have appeared suddenly and have gradually subsided upon discontinuance of therapy. Since the onset of the overloading syndrome may be preceded by a persistent and increased lipemia, examination of the fasting serum for residual turbidity may be a useful means of detecting impending reactions; cottonseed oil infusions should be discontinued if a gross serum turbidity (lipemia) persists for 18 to 24 hours after the last infusion. If prolonged therapy is contemplated, repeated complete hemograms should be done. Since the syndrome can occur even in the absence of gross lipemia, the patient should also be closely observed for premonitory signs and symptoms such as rising temperature, anorexia, abdominal pain, hepatomegaly, splenomegaly, and any evidence of abnormal bleeding. Liver function tests, particularly sulfobromophthalein retention, may also be helpful as an indicator of approaching intolerance. Although the available evidence indicates that effects of intravenous fat emulsions on the liver are temporary or reversible, such therapy should be undertaken cautiously in patients with severe liver disease or in those with a history of thromboembolic or other cardiovascular disease.

Dosage.—Cottonseed oil emulsion is administered only by intravenous drip. It should not be mixed with blood, fluids, or any other parenteral medication or given simultaneously through the same tubing. Either one or two infusions of 250 cc. or 500 cc. each of a 15% emulsion are given each day, depending on the caloric requirements of the individual patient and taking into account the intake by other means. To minimize immediate reactions, the rate of infusion must be extremely slow. For adults, infants, and children, no more than 10 drops (0.5 cc.) per minute should be infused during the first five minutes. For the next 25 minutes, the maximum rate of infusion for adults is 40 drops (2 cc.) per minute. Thereafter, the emulsion may be infused at a rate of 100 drops (5 cc.) per minute. After the initial five minutes, the maximum rate of infusion for infants and children is one-half to one drop per pound of body weight per minute, the maximum daily dose ranging up to 10 cc. per pound of body weight.

Sufficient evidence is not at hand to permit recommending therapy with this cottonseed oil emulsion beyond the maximum of 14 infusions of 500 cc. each.

Preparation: emulsion (injection) 15% in 250 cc. and 500 cc.

The Upjohn Company cooperated by furnishing scientific data to aid in the evaluation of cottonseed oil emulsion.

Vancomycin Hydrochloride (Vancocin).—The hydrochloride salt of an antibiotic substance obtained from strains of Streptomyces orientalis. The structural formula of vancomycin hydrochloride has not been determined.

Actions and Uses.—Vancomycin hydrochloride, introduced in 1958, is an antibiotic which is highly active against gram-positive cocci. The drug is bactericidal, in vitro and in vivo, for streptococci, pneumococci, and staphylococci. Vancomycin is excreted in the urine; its metabolic fate and distribution are not known.

Vancomycin hydrochloride administered intravenously has proved to be valuable for the treatment of certain severe staphylococcic infections. In a number of instances, it has undoubtedly been lifesaving. The drug is not intended for routine use, nor should it be used in mild infections. Instead, it should be reserved for critically ill patients with life-endangering infections produced by strains of staphylococci which are resistant to the antimicrobial action of the commonly used antibiotics. Because of the specificity of vancomycin against such infections, it is particularly valuable for use in hospitals in which so-called antibiotic-resistant staphylococcic infections are becoming an increasingly serious problem. To date, no instance of natural or acquired staphylococcic resistance to vancomycin has been reported, either in vitro or in vivo. Neither has cross resistance to other antibiotics been observed. If, in the light of subsequent clinical experience, all strains of the organism remain uniformly susceptible to vancomycin, this antibiotic may well become the drug of choice for the treatment of severe staphylococcic infections which fail to respond to other antibiotics. The indiscriminate use of vancomycin is, in large measure, discouraged by the fact that it must be administered intravenously.

Vancomycin hydrochloride has also been used in the treatment of severe infections produced by penicillin-resistant strains of alpha or nonhemolytic streptococci. In a number of patients with subacute bacterial endocarditis due to such organisms, the drug has produced gratifying results. There appears to be little justification for its use in beta hemolytic streptococcic or pneumococcic infections since these invariably respond well to therapy with penicillin.

The toxicity of vancomycin hydrochloride is minimal for most short-term therapy. The drug can, however, produce an impairment of auditory acuity, especially when therapy is prolonged or when large doses are given. In the presence of severely impaired renal function, the excretion of vancomycin is decreased and the drug accumulates in the blood. Since this may enhance the likelihood of ototoxicity, the drug should be used with considerable caution in patients who have renal damage. Periodic determinations of the blood urea nitrogen level are likewise suggested for all patients receiving doses greater than 2 Gm. per day. Vancomycin hydrochloride is irritating to the venous endothelium and may cause pain at the site of intravenous injection; chemical thrombophlebitis has been observed when concentrated solutions were used or when the drug was administered repeatedly into the same vein. Macular skin rashes and febrile reactions have been encountered.

Dosage.—Vancomycin hydrochloride is administered only by the intravenous route. For adults, the usual dose for a 24-hour period is 2 Gm. This is generally administered in amounts of 500 mg. every six hours, although some investigators have found it feasible to give only two infusions of 1 Gm. each at 12-hour intervals. Higher doses of 3 to 4 Gm. daily should be used only in desperately ill patients who have normal renal function. The daily dosage for children is 20 mg. per kilogram of body weight.

Concentrated solutions of the drug, containing 500 mg. in 10 cc., can be given by direct intravenous injection over a period of four to five minutes. Preferably, however, this concentrated solution should be diluted with 100 to 200 cc. of isotonic sodium chloride solution or 5% dextrose in water for injection and infused by intravenous drip over a period of 20 to 30 minutes.

Preparations: solution (injection) 500 mg. in 10 cc.

Eli Lilly and Company cooperated by furnishing scientific data to aid in the evaluation of vancomycin hydrochloride.

SEX DISTRIBUTION OF LEPROSY.—It is still taught and believed that leprosy is characteristically commoner among males, but some of the figures produced need to be seen against their background. Nearly twice as many men attend hospitals in this country [East Africa] as women, but there are not twice as many men nor are they sick twice as often. The women are simply less mobile. . . . The over-all lepromatous rate was 9.1% but significantly more males had lepromatous leprosy, and more females tuberculoid or non-lepromatous leprosy. . . . Where leprosy is more common among males, the lepromatous type predominates; where the tuberculoid type is more common, more females are infected. This was the experience in Southern Nigeria. It is true of Uganda and of parts of Kenya. . . . Somewhere there must be an endocrine link, lepromatous leprosy being the "masculine type" and tuberculoid leprosy the "feminine type." . . . The same or a related endocrine influence may be associated with the higher male and lepromatous ratios which exist at the present time among races whose skins are less pigmented than the Africans. The sex-type distributions may thus indicate the stage and trend the disease has reached. They may be the consequence of endocrine adaptation, the method or result of successful defence. The differences in the disease patterns are characteristics not of the disease any more than they are superficially of the race, but of a particular group of individuals within the race. The adaptation which takes place is probably a long-term process whereby a less infectious type of disease is produced, a form of natural selection.—J. A. Kinnear Brown, B.Sc., M.D. Factors Influencing the Transmission of Leprosy, *Transactions of the Royal Society of Tropical Medicine and Hygiene,* March, 1959.

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MEDICAL EXAMINER VERSUS CORONER

GUEST EDITORIAL

Alan R. Moritz, M.D.

WHETHER the title of office is coroner or medical examiner is unimportant. It is important, however, that the office holder be qualified to discharge the one essential function of his office and that he have the necessary authority and assistance to do so. That function is to investigate all deaths in his jurisdiction that have occurred unexpectedly from obscure causes or that have been caused by violence for the purpose of getting such medical facts as may be required for the administration of justice and for the preservation of public safety.

The failure of the coroner or the medical examiner to obtain and to interpret correctly the medical and paramedical evidence in such cases predisposes to (*a*) suspicion or prosecution of innocent persons when death from disease or misadventure has occurred in circumstances such as to simulate homicide, (*b*) nonrecognition of homicide when the circumstances and the appearance of the body are such as to simulate death from natural causes or misadventure, (*c*) nonrecognition of the fact that death was due to occupational injury or disease with consequent injustice to surviving dependents, or (*d*) nonrecognition of unsuspected hazards to public health. These are not merely theoretical possibilities. They are the inevitable results of an inadequate medicolegal investigative system.

What is a coroner? In most states he is a county official who has been elected to office through the machinery of partisan politics. Usually he is not required to be a physician. As a rule he does not have the authority, the facilities, or the appropriation necessary to conduct competent medicolegal postmortem investigations even though by chance he may have the requisite knowledge and desire to do so. Despite these generalizations there are several excellent coroner's offices in the United States.

What is a medical examiner? Ordinarily he differs from the average coroner in several important respects. The first is that he is invariably a physician. The second is that he usually achieves office under some form of merit system rather than by election on a partisan ballot. In the jurisdictions where the change from coroner to medical examiner has occurred during the past 20 years the latter is usually required to be a pathologist. Because the laws pertaining to the office of medical examiner are relatively modern he characteristically has greater authority, better facilities, and a more nearly adequate appropriation. Ordinarily the inquest and various other nonmedical functions of the coroner's offiice are either abolished or transferred to some other agency of county government when the office of coroner is replaced by that of medical examiner. It should be emphasized that a change of name from coroner to medical examiner does not of itself improve the situation.

During the past decade two outstanding studies of the problem of coroner versus medical examiner have been made and each has resulted in the drafting of model legislation. The first of these, entitled "A Model State Medico-Legal Investigative System," was the subject of a joint report by the American Academy of Forensic Sciences, the American Bar Association, the American Judicature Society, the American Medical Association, the National Civil Service League, and the National Municipal League and was published in 1951 by the National Municipal League.

The second, entitled a "Model Post-Mortem Examinations Act," was prepared and approved by the National Conference of Commissioners on Uniform State Laws and was published in 1954. It is urged that the various county and state medical societies appoint committees to examine the needs of their respective coroner's or medical examiner's offices with a view to initiating and supporting such legislative changes as are required to improve this potentially important bulwark of justice and public safety.

Copies of "A Model State Medico-Legal Investigative System" and "Model Post-Mortem Examinations Act" may be obtained by writing to the Committee on Medicolegal Problems of the American Medical Association, 535 N. Dearborn St., Chicago 10.

From the Institute of Pathology, Western Reserve University, Cleveland.

MEDICINE AND THE LAW

COVERAGE AND EXCLUSIONS OF PROFESSIONAL LIABILITY INSURANCE

This study of professional liability insurance is intended to point out certain areas of uncertainty and doubt which exist with respect to coverage and exclusions in standard medical professional liability insurance policies. Discussions among physicians about professional liability insurance have usually been in terms of high-limit versus low-limit coverage. The unfortunate physician who is faced with a $50,000 claim and has only $25,000 in coverage has just cause to be unhappy, but not any more so than the physician who discovers that the plaintiff's claim is excluded by the terms of his policy.

Contrary to the popular impression, professional liability insurance does not provide all-risk coverage. The opinion has been expressed that the ethical physician is amply protected; that only the unethical physician who guarantees cures which are improbable, the abortionist who performs illegal operations, or the narcotics addict or alcoholic who renders treatment while under the influence of narcotics or alcohol need be concerned about exclusions in his policy. The fact is that the ethical physician who is wrongfully accused of such conduct may find that he is without defense or coverage. Furthermore, there are limitations with respect to certain areas of medical practice which, to varying degrees, are restricted in some policies. Disputes between physicians and their insurers have occurred, and in some instances the result has been litigation which has gone as far as the appellate courts.

Purchasing Malpractice Insurance

Professional liability, in common with other forms of insurance, may be purchased through agents or brokers. The agent is a representative of the insurance company. Generally, he may countersign and deliver policies and make collections in the name of the company. The broker is a representative of the purchaser. The same person may be an agent for some companies and serve the insurance buyer as a broker with respect to other companies.

In buying any kind of insurance it is wise to select a company with substantial reserves and unassigned surplus that has stood the tests of time. This is particularly true of medical professional liability insurance. The patient whom the doctor treats today may bring a malpractice action many years from now, and the doctor will want every reasonable assurance that his present insurance carrier will be in business and able to afford him the protection for which he has paid. The statute of limitations against the claims of minors does not begin to run until they have attained their majority, and in many states the statute does not begin to run against adults until the existence of a malpractice injury has been disclosed.

It is also desirable to buy insurance from a company that is licensed to do business in the state where the insured is engaged in practice. The insurance industry is regulated under the laws of the various states through state insurance departments. Although the United States Supreme Court in *United States v. South-Eastern Underwriters Association* [1] held that insurance is interstate commerce and subject to federal regulation, the federal government has not seen fit to enter this field of government regulation.

In order to be licensed to do business in a particular state an insurance company must make application and qualify financially. The company becomes subject to the insurance laws of the state and to the rules and regulations of the state insurance department. These rules generally provide for prior approval of the provisions contained in insurance policies and the protection of the public against arbitrary refusal of the company to fulfill its contractual responsibilities under the policies which it issues. The state insurance department will act on the complaint of a policyholder in cases in which it appears that a company is not acting in good faith under the terms of its insurance contract.

Policy Provisions

The medical professional liability policy is usually divided into three sections, insuring agreements, exclusions, and conditions.

The insuring agreements state the coverage provided by the policy. The company agrees to pay on behalf of the insured damages because of injury arising out of malpractice by him in rendering or failing to render professional services. The company also agrees to defend any suit against the insured alleging such injury. Unless an additional premium is paid for such coverage, damages resulting from the contingent liability for the malpractice of a partner are excepted. The company in most instances reserves the right, with the written consent of the insured, to settle any claim or suit as the company deems expedient. One policy provides that settlement may not be made without the consent of the insured; but, if the physician refuses to approve a settlement offer when acceptance is recommended by the company, the insurance coverage is automatically limited to the amount of the settlement offer.

The exclusions usually state that the policy does not apply to (*a*) such risks as injury arising out of the performance of a criminal act; (*b*) injury caused by a person while under the influence of intoxicants or narcotics; (*c*) liability assumed by the insured under an agreement guaranteeing the result of any treatment; (*d*) x-ray apparatus used for therapeutic treatment (unless specifically included in the policy at an additional premium); or (*e*) liability of the insured as the proprietor or executive officer of a hospital or sanitarium.

In addition to the foregoing standard exclusions the Law Division of the American Medical Association noted in examining sample policies issued by the various insurers that some of the companies also exclude one or more of the following contingencies: shock therapy, cosmetic plastic surgery, contact lenses, nonpathological sterilization, the acts of any non-M.D. anesthesiologist, the use of hand fluoroscopes, nuclear energy liability, or the employment of any surgeon without the knowledge and consent of the patient.

The conditions contain such provisions as a statement referring to the monetary limits of the policy and the duty of the insured to notify the company promptly in event of a claim or suit and to cooperate with the company in defending any claim or suit. Also, the insured may cancel the policy at any time, whereas 10 days' written notice of intent to cancel is required on the part of the company. Some policies require 30 days' notice of cancellation on the part of the company, and a few group policies may be cancelled only at the end of the policy year.

Insuring Agreement

Most of the companies that write professional liability insurance in the United States use the form of the Physicians', Surgeons', and Dentists' Professional Liability Policy adopted by the National Bureau of Casualty Underwriters and referred to in this article as the "standard" policy. The coverage provision in this form states that the company agrees:

> To pay on behalf of the insured all sums which the insured shall become legally obligated to pay as damages because of injury arising out of malpractice, error or mistake in rendering or failing to render professional services in the practice of the insured's profession described in the declarations, committed during the policy period of the insured or by any person for whose acts or omissions the insured is legally responsible except as a member of a partnership.

The insuring clauses contained in the policies issued by other companies are generally to the same legal effect.

Coverage is not limited to injuries to patients. The insurance would apply to a husband who sues for loss of his wife's services and should also apply to other persons who might be injured by the physician in rendering professional services. For example, if, in the course of performing a particular procedure, the physician's instrument should slip and he should injure the patient's parent who is standing by, the physician should be entitled to insurance protection with regard to the liability thereby incurred.

The insurance protection is not restricted to particular kinds of injury. "Injury" accordingly may include bodily injury, property damage, personal restraint, undue familiarity, and other forms of personal injury such as libel, slander, mental anguish, and invasion of privacy. A few forms specifically itemize assault and battery, breach of implied contract, and libel and slander in the insuring clause. The fact that the National Bureau form of insuring clause does not list the specific causes of injury arising out of professional practice for which a physician may be sued would not appear to denote a narrower area of coverage.

However, it should be emphasized that coverage exists only with reference to injuries which arise out of the insured's profession. A physician's liability policy was held not to cover a judgment against the insured as county coroner for an unlawful autopsy examination performed at his direction as coroner in *Crenshaw v. U. S. Fidelity & Guaranty Co.*[2]

The partnership liability which may be created because of malpractice committed by a partner is specifically excepted. For an additional premium it is the usual practice for malpractice insurers to provide such protection. Physicians who are in partnership practice are responsible for each others' acts and are not protected unless contingent partnership liability coverage is stated in the policy. Such coverage can be particularly essential in the event a malpractice claim is made against a partner who dies or if a malpractice judgment is rendered against a partner who does not have adequate coverage to meet the judgment.

Cases Involving Disputed Coverage

Equipment.—In *American Policyholders Ins. Co. v. Michota*[3] a patient had gone to a chiropodist for treatment of a foot ailment. The doctor instructed her to sit in a metal hydraulic chair designed for the occupancy of patients. Due to the failure of the chiropodist to "lock" the chair it suddenly rotated as she was attempting to get into it, throwing her to the floor and injuring her.

In an action to determine if the insurer was liable to the chiropodist for the amount of a judgment obtained against him by the patient, the insurer contended that the policy was strictly limited to those injuries which might arise out of the actual rendition of professional services and that injury due to the condition of the chair was not covered. The court held that the injury was one "arising out of the practice of the insured's profession" and also constituted "an injury resulting from professional service rendered or which should have been rendered," which brought it within the coverage of the insured's professional liability policy. The court said that maintaining the treatment chair in a proper and safe condition for the accommodation of patients was a service or duty directly connected with the practice by the insured of his profession as a chiropodist.

The term "malpractice, error, negligence, or mistake" was held in *Harris v. Fireman's Fund Indemn. Co.*[4] to cover injury to the patient of an insured osteopath when the safety catch on his treatment table failed, causing collapse of the table.

Libel.—In *Maier v. U. S. Fidelity & Guaranty Co.*[5] the plaintiff was a member of the Colorado State Medical Society, which carried group insurance with the defendant insurer. He sued the insurance company to recover attorney's fees and costs expended in defense of a libel suit.

About June, 1946, the insured had signed a death certificate, and, after supplying all of the necessary medical information, he added in the margin the following statement: "This patient died from criminal neglect at the [blank] Sanitarium." In June, 1950, suit was instituted by the sanitarium based on two claims, one of which referred to the above marginal statement written by the insured and the other to a publication in a newspaper, about three years after the death certificate was signed, of a photostatic copy of the death certificate together with the statement that the patient had died after being at the sanitarium for several years without care. This litigation terminated favorably to the insured.

The physician then brought suit against the insurer to recover his expenses. The policy insured the physician against any claim or suit based on malpractice, error, negligence, mistake, slander, or libel arising from his professional services. The insurer had offered to provide defense only for the first cause of action in the sanitarium case, but this was refused by the insured and his attorney. The court held that when the insured rejected this offer and hired counsel, in violation of a policy provision that he would not contract any expense without the insurer's written authorization, he was not entitled to recover from the insurer for attorney fees and costs.

As to the second cause of action in the sanitarium case, concerning the publication of the alleged libel in the newspaper, this was not covered by the insured's policy since it was not related to professional services rendered or which should have been rendered. The court said:

> When the insurer offered to defend the first cause of action and was refused, the insured insisted that the defense should be conducted by an attorney of his choosing, such choice on the part of the insured was one that he had no right to make under the terms of the policy. There is little doubt, if any, that there was liability on the part of the insurer to defend that part of the . . . suit based upon the marginal notation of the death certificate, but no liability as to the other. While it is true that the marginal notation on the death certificate was not a pure compliance with any requirement of the law or the death certificate itself, it may be considered as an allowable elaboration of the insured's full diagnosis of the causes of death.

Period of Coverage

In a case in which the treatment of a patient began before a professional liability policy became effective but is continued thereafter for some period of time, the insurer will be liable to defend a suit if it is claimed that acts of malpractice occurred after the effective date of the policy. In *Aetna Life Ins. Co. v. Maxwell*[6] a physician treated a patient from March 26 to Aug. 7, 1932. The policy of insurance against malpractice was issued on July 23, 1932. It was held that the defendant insurance company was liable only for such malpractice or neglect as took place between July 23 and Aug. 7. Since it was necessary for the jury to distinguish between the effects of the medical and surgical treatment before and after July 23, the court of appeals ruled that it was error for the trial court to exclude offered medical expert testimony on this issue.

In *Shaw v. U. S. Fidelity & Guaranty Co.*[7] the patient received 41 treatments prior to the issue of the policies of insurance. Only 14 treatments were given after the policies were in force. The insurance company took the position that the patient's injuries were caused by the treatments received prior to the inception of the insurance coverage and not by the treatments received thereafter. The court stated that the company would be liable if it was shown that the injuries received by the patient were sustained by her as a result of the 14 treatments last given to her, and also that the company would be deemed liable if the 14 treatments last given caused the patient's injuries because their effect was added to that of the 41 treatments first given.

The original policy issued to the insured covered the period from Nov. 20, 1925, to Nov. 20, 1926, and the second policy covered the period from Nov. 20, 1926, to Nov. 20, 1927. The patient noticed ill-effects from her treatment for the first time in August, 1926, and there was conflicting testimony on the question of whether the injuries were sustained within the period of the policy. The court held that the question of the weight and sufficiency of this testimony was properly left to the jury.

In *Waterman v. Fidelity & Casualty Co.*[8] an insured physician began treatment of a patient on Feb. 20, and the liability policy was issued on March 18. The physician continued to treat the patient for five or six weeks thereafter, and in a subsequent case brought by the patient against the physician for malpractice it was alleged in the complaint that the physician had continued to treat the patient after the policy was issued, during all of which time he was guilty of malpractice.

The court held that the insurer should have defended the case for the insured, and that not having done so it was liable to reimburse the insured for the amount he had been required to expend as the result of the suit. The contention of the insurer had been that since the patient was first treated on Feb. 20, which was prior to the issue of the policy, the malpractice was not within the scope of the coverage. The court, however, dismissed this contention, stating that it had been expressly charged in the malpractice case that the plaintiff had been guilty of malpractice while the policy was in force.

Guaranteed Result

Suits in which the patient claims that a guaranteed result was not obtained present a particular hazard to the doctor, because they are specifically excluded from coverage in professional liability policies. Evidence of a poor result is sufficient to justify a verdict if the jury chooses to believe that an oral agreement of guarantee had been entered into. When malpractice is charged expert medical testimony is generally necessary to support the claim that the doctor failed to exercise the proper degree of *skill*, but in a contract action the doctor's *skill* is not in issue.

An overly optimistic prognosis may lead some patients to believe that the physician guarantees a satisfactory result, and, if taken literally, his careless remarks may give rise to the semblance of a contract of guarantee which he does not intend. Assuming, for example, that the patient is suffering from a painful condition which can be cured by an operation which statistically involves a minimum operative risk, and because even the most prudent, informed persons might be expected to undergo such surgery as a matter of course, the surgeon may unwittingly go too far in attempting to convince the patient. "I assure you that you will be good as new," or "I guarantee you that this operation will make you well again," are remarks that may have the legal purport of a contract of guaranteed cure. Yet they may be taken out of the context of a fuller conversation that is intended solely to convince the patient to undergo an operation that any reasonable, intelligent, and informed person would not hesitate to risk. But what if despite skillful surgery the patient turns out to be the one unfavorable statistic out of a thousand?

In agreeing to perform an operation, the physician does not, in the absence of a special contract, guarantee particular results or cure.[9] In only a few of the published cases in which a guaranteed result was alleged was there any legitimate basis to claim the existence of a contract guaranteeing a cure. However, since such claims are excluded from coverage by the standard policy, a physician-defendant in such an action is entitled to neither indemnification nor defense.

The studies of the A. M. A. Law Division show that, by and large, physicians of reputable standing in the medical community are the ones generally involved in malpractice actions. The exclusion against guaranteed results may be intended to safeguard the insurance company that inadvertently issues a policy to a quack. Nevertheless, it operates to deprive the reputable and qualified physician of insurance coverage, if he unwittingly makes remarks which the plaintiff and the jury or court choose to construe as a contract of guarantee, or if he is the target of an unscrupulous plaintiff.

Howard Hassard,[10] *a California attorney who is* prominent in defending physicians' malpractice cases, recently reported that "suing for breach of contract has become popular of late among plaintiffs' lawyers." Here, then, is an area of potential liability in which the doctor is faced with a serious unprotected gap in his insurance coverage. From the standpoint of the medical practitioner the standard policy should be revised to provide him with defense against a claim or suit charging a guaranteed result and also indemnification for payment of the judgment unless the findings of the court show that he was guilty of conduct amounting to a violation of the principles of medical ethics.

In *Safian v. Aetna Life Ins. Co.*[11] the court held that a policy indemnifying a physician against loss for claims for damages "on account of any malpractice, error or mistake committed" by the physician did not cover liability in an action for breach of an oral contract to remove facial blemishes. One of the statements in connection with the issue of the policy was the representation made by the physician that he did not have in force and would not "enter into any special contract or agreement . . . guaranteeing the result of any operation or treatment." The court said:

> It should be obvious that insurance coverage for claims arising out of "malpractice, error or mistake," is clearly legally distinguishable from coverage for breach of contract. The legal duty, the breach of which is covered is wholly different. If a doctor makes a contract to effect a cure and fails to do so, he is liable for breach of contract even though he used the highest possible professional skill. Insurance of such a contract could protect only medical charlatans. The honorable member of the medical profession is more keenly conscious than the rest of us that medicine is not an exact science, and he undertakes only to give his best judgment and skill. He knows he cannot warrant a cure.

In *McGee v. U. S. Fidelity & Guaranty Co.*[12] a physician was found to have entered into an oral special contract with a patient whereby he guaranteed to perform a skin graft operation which would give the patient "a perfect hand." The court held that a policy protecting the physician against losses due to malpractice did not cover a loss suffered when the physician was sued because of an alleged disfigurement in an attempted skin graft, since the liability arose out of the special contract to perfect a cure with a guaranteed result, and not because of "malpractice, error or mistake" in treatment. The physician's liability did not result from the implied contract applicable to every physician in the treatment of his patient, which is covered by malpractice insurance, but because of the special contract to give his patient "a perfect hand."

A different result was obtained in *Sutherland v. Fidelity & Casualty Co.*[13] The physician's policy insured him against liability for malpractice, error, or mistake in the practice of his profession, and against loss from the liability imposed by law on the assured for damages on account of bodily injuries or death, suffered by any person or persons in consequence of any malpractice, error, or mistake. The court held that this covered an act of liability based on a contract entered into between the assured and his patient, whereby the former agreed to remove all the gallstones and causes of disease from the latter, which was not successfully accomplished. The insurer argued that the phrase "liability imposed by law" referred only to common-law liability and not to that which had its basis in contract. The court rejected this contention, stating that such reasoning would be sound only if the policy had covered malpractice alone, but that it clearly did not apply when the coverage was extended to mistake or error. The court concluded that the fact that the insured had entered into a special contract did not affect the insurance policy, because it was a contract made in the practice of his profession and one which he clearly had a right to make.

Criminal Acts

When the patient's injuries were attributable to the use by the insured physician of an unqualified and unlicensed assistant in violation of the provisions of law, the court in *Glesby v. Hartford Accident & Indem. Co.*[14] held that the liability of the insured for malpractice in the treatment of the patient was not within the coverage of the policy. The policy provided that it would not cover bodily injuries caused by the assured or any assistant of the assured while engaging in a violation of any law or ordinance.

Many of the actions brought by patients against physicians allege assault and battery[15] and not necessarily a charge that the physician negligently failed to render services with the requisite degree of skill. These cases usually involve a claim that a surgeon operated without proper consent or that he extended the operation beyond the consent given. Even though the surgeon may have acted in complete good faith, doing what he believed to be in the best interest of the patient, lack of legal consent amounts to a technical assault and battery and, subject to local law, may be construed as an unlawful or criminal act.

In *Shehee v. Aetna Cas. & Sur. Co.*[16] a federal district court in Louisiana held that the failure to obtain a patient's consent before performing an operation did not constitute assault and battery, as that term was intended in the exclusionary clause in the policy in question which excluded acts involving "assault and battery" from coverage by the policy. The court reasoned that liability was covered under the insuring clause covering acts of malpractice.

Failure to obtain a proper consent to an operation has nevertheless been repeatedly held to constitute assault and battery in actions brought by patients against physicians for civil damages. If the philosophy of the *Shehee* decision is applied in interpreting the policy exclusion of "injury arising out of the performance of a criminal act," the exclusion would operate only in those cases in which it would offend public policy or good conscience to require the insurer to indemnify the policyholder. For example, if a physician were to deliberately assault and injure a patient who refused to pay a bill for services, the criminal act exclusion would avoid coverage. However, it is unlikely that an injury of this nature could be considered as arising out of the rendition of professional services, as required by the insuring clause.

It may be contrary to public policy for an insurer to be required to indemnify a physician convicted of illegal abortion for any civil damages that he might be required to pay. But the policy exclusion of criminal acts is far broader than necessary to satisfy public policy. A convicted abortionist should not be able to satisfy his civil liability through insurance, but the term "criminal act" embraces misdemeanors as well as felonies, and intent to do wrong is not necessarily an ingredient of the criminal act. Furthermore, the insurance company may determine for itself whether the plaintiff's claim involves a criminal act committed by the doctor. The prior judgment of a court is not necessary.

To provide the reputable physician with unambiguous and adequate insurance protection the exclusion of criminal acts should be qualified. Defense should be required except in cases in which the act involved is one for which the physician has been convicted by a criminal court. Obviously there should be no indemnity where the court has found that an illegal abortion occurred, nor where the laws of the state may prohibit indemnity for reasons of statutory law or public policy. A further exception excusing indemnification might be with reference to an act found, by the court, to have been committed by the physician-defendant which is in violation of the principles of medical ethics.

Misrepresentation

The company may deny liability in a loss situation in which a material fact, one that would have affected the issue of the policy, was deliberately misrepresented. In *U. S. Fidelity & Guaranty Co. v. Fridrich*[17] a dentist represented himself as a member in good standing of his state dental society at the time of securing the policy. His acceptance of a renewal of his policy was held to be a new representation to the same effect, and if, at that time, he had failed to pay dues and was not in good standing, the insurer has been held entitled to cancel the policy. The court said: "A part of the consideration for the policy was membership, and when this condition of membership did not exist the consideration failed." The insurance company issued different policies for members of the state dental society and for nonmembers.

Reservation of Rights

An insurance company may do one of the following things when it is notified of a claim or suit against a policyholder. 1. It may assume its responsibilities under the policy without raising any question as to coverage. 2. The decision may be made that the claim is not covered by the policy, and the company may send the policyholder a notice of disclaimer of liability. 3. The insurer may preserve the status quo as to its defenses by sending the policyholder a letter of reservation of rights, or by requiring a nonwaiver agreement to defend.[18]

A notice of reservation of rights is a notice from the insurer that it will investigate the claim, defend any suit, discuss settlements with the claimant, or take any other action, with reference to the claim, without waiving its rights under the policy. The company will probably say that it reserves the right at any time to discontinue the investigation, defense, discussion of settlement, or other action and disclaim liability.

In the event of a dispute between the insured and the insurance carrier regarding coverage the company may ask the insured to sign a nonwaiver agreement. This agreement permits the company to proceed to handle the claim and defend any suit without surrendering the company's right to later disclaim liability under the policy.

Cooperation

The policy requires the assured to assist and cooperate with the insurance carrier. The standard provision states:

> The insured shall cooperate with the company, and, upon the company's request, shall attend hearings and trials and shall assist in effecting settlements, securing and giving evidence, obtaining the attendance of witnesses and in the conduct of suits. The insured shall not, except at his own cost, voluntarily make any payment, assume any obligation, or incur any expense.

The insurance company is entitled to a full, frank, and truthful disclosure of all the facts. The insured's liability to cooperate with his insurer was ably stated by Judge Cardozo in *Coleman v. New Amsterdam Casualty Co.*[19]:

> "Cooperation with the insurer is one of the conditions of the policy. When the condition was broken, the policy was at an end, if the insurer so elected. . . . Cooperation does not mean that the assured is to combine with the insurer to present a sham defense. Cooperation does mean that there shall be a fair and frank disclosure of information reasonably demanded by the insurer to enable it to determine whether there is a genuine defense. . . ."

It is the duty of an insured person to cooperate with the company by appearing at the time of trial and assisting therein. In *Medical Protective Co. v. Light*[20] it was held that the insurer was obliged to pay the traveling expenses of the insured physician in attending the trial, but he would have no right to make a professional charge for attendance as a witness. The policy stated that the insured "will attend, assist, and cooperate . . . without charge." The insured physician lived in Texas and the case was tried in Ohio where the alleged malpractice had occurred and where he had formerly practiced.

Settlement

When a claim is made the insurance company will conduct an investigation and then estimate the reasonable disposal value of the claim. A reserve in this amount for the payment of the claim is established, inasmuch as claims reserves are generally required by state insurance laws to assure the availability of funds to pay claims. Whether the claim will be settled within or in excess of the original reserve or allowed to mature into a lawsuit is determined by subsequent developments and negotiations.

The standard settlement provision states that the company may make such investigation and negotiation and, with the written consent of the insured, such settlement of any claim or suit as the company deems expedient.

This provision gives the physician protection against the settlement by the insurer of unmeritorious claims. Unfortunately, there are some attorneys who will press for settlement of claims which they know could not be successfully substantiated in court. Solely from the standpoint of cost it may be cheaper for an insurer to dispose of these nuisance claims by way of a nominal settlement rather than to incur the expense of defending a lawsuit. As a matter of principle, the average physician will resent any payment to dispose of an invalid claim. Furthermore, many physicians feel that any malpractice claim that is settled reflects adversely against their professional reputations.

However, no physician should as a practical matter refuse an insurance company's decision to settle a claim unless he has first secured the advice of his personal attorney. A refusal to settle within the limits of the policy may result in a judgment in excess of the policy limits, in which case the physician would be obliged to pay the excess. The question is probably academic, but if a doctor were arbitrarily and unreasonably to prohibit an insurer from settling an obviously valid claim at a low figure, he might have to contribute the difference between this amount and the judgment rendered by the court, even though the judgment was within the policy limits.

Another form of policy provides that:

> The Underwriters shall not settle any claim without the consent of the Insured Person. If, however, the Insured Person shall refuse to consent to any settlement recommended by the Underwriters and shall elect to contest or continue any legal proceedings in connection with such claim, then the liability of the Underwriters for the claim shall not exceed the amount for which the claim could have been so settled plus the costs and expenses incurred with their consent up to the date of such refusal.

This settlement provision does not permit the insurer to settle without the insured's consent, but refusal to consent could be costly. For example, if a claim could have been settled for $500, but the insured refused to permit settlement, this amount fixes the maximum responsibility of the insurer with reference to the claim and subsequent costs. Assuming that the claim is defeated, but $1,500 is subsequently spent in defense and litigation costs, a literal interpretation of the language of the policy might make the insured responsible for the $1,000 difference in the cost of disposing the claim.

The liability of an insurer is generally limited to the amount stated in the policy. Under exceptional circumstances insurance companies have been held liable for amounts in excess of policy limits. Such cases involve negligence, fraud, or bad faith on the part of the company in refusing an offer to settle within policy limits with a subsequent court verdict in excess of policy limits. However, there are no reported cases involving professional liability insurance in which an insurer has been held liable in excess of policy limits.

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GOVERNMENT SERVICES

AIR FORCE

Medical Aspects of Missile Operation Course.—The Air Force Medical Service will train personnel from the three military services in the medical and occupational health problems occurring in missile launching operations. The 10-day Medical Aspects of Missile Operation course will be held at Cape Canaveral, Patrick Air Force Base, Fla. Five courses will be held each fiscal year with 25 students from the military services attending each course. This course is designed to meet the new environmental medical problems arising from the rapid advances of the missile development program and the associated revolutionary changes in military operations at missile sites.

Course in Space Medicine.—In September the first advanced course in aerospace medicine for senior medical officers from allied nations will begin at the U. S. A. F. School of Aviation Medicine, Randolph Air Force Base, Texas. The 27-week course will consist of academic aviation medicine, a physiological training program, and practical aspects of aviation medicine. The quota for each class is 15 students. To be eligible students must have completed the primary course in aviation medicine at the U. S. A. F. School of Aviation Medicine or a comparable course in their respective countries.

Personal.—Col. Larry A. Smith, U. S. A. F., M. C., will become director of medical staffing and education, Office of the Surgeon General, U. S. A. F., on June 30. He replaces Brig. Gen. M. S. White, U. S. A. F., M. C., who has been assigned as surgeon of the Air Training Command. Col. William F. Patient, U. S. A. F., M. C., will become surgeon of the Alaskan Air Command on June 30. He replaces Brig. Gen. John R. Copenhaver, U. S. A. F., M. C., who has been assigned as surgeon of the Tactical Air Command.

NAVY

Personal.—Rear Adm. Irwin L. V. Norman, Medical Corps, U. S. Navy, Inspector General of Medical Department Activities, retired from active naval service on April 30. Admiral Norman had more than 31 years of active service. . . . Rear Adm. John Q. Owsley, Medical Corps, U. S. Navy, Inspector of Naval Medical Activities, Pacific Coast Headquarters, Western Sea Frontier, since April, 1958, also retired after a naval career of more than 34 years. . . . Capt. George N. Raines, Medical Corps, U. S. Navy, Head of the Neuropsychiatric Branch, Bureau of Medicine and Surgery, retired after more than 28 years of active service. . . . Capt. Thomas M. Manley, Medical Corps, U. S. Navy, of the Naval Air Station, Minneapolis, retired after 17 years of active service. . . . Capt. William R. Whiteford, Medical Corps, U. S. Navy, of the Naval Station, Long Beach, Calif., retired after more than 30 years of active service.

VETERANS ADMINISTRATION

Rehabilitating the Aged.—An effective medical approach to overcoming the disabilities of old age is being pioneered in Veterans Administration hospitals. Essentially an adaptation of rehabilitation techniques developed for veterans after World War II, the treatment is keyed to both emotional and physical aspects. Through exercise of both body and the mind, even oldsters with severe disabilities often are enabled to care for themselves to some degree. At the Dayton, Ohio, VA center, nurses, nursing assistants, ward secretaries, psychologists, and other staff members unite with physicians in a team approach. This program has proved so successful that Ohio State Health Department public health nurses and others are visiting the hospital to observe the rehabilitation techniques.

With an average daily patient load of about 111,000 veterans, nearly half of whom are 55 years or older, the VA's 171 hospitals have a heavy responsibility for development of treatment of this sort. This program begins where usual medical treatment for acute illnesses leaves off, is planned to consider the needs of the whole person, and draws on the services of the entire hospital staff and of volunteers. Responsibility for the sick and disabled veteran includes promotion of a more effective philosophy in the community toward the process of aging and the illnesses that accompany it. Aging disabled veterans are thereby enabled to spend their remaining years outside of hospital wards.

Unusual Art Exhibit.—One of the most unusual collections of paintings in the nation soon will be hung in the national headquarters of the American Psychiatric Association in Washington, D. C. Entirely the work of psychiatric patients in art therapy clinics of Veterans Administration hospitals, the 24 paintings were chosen by James McLaughlin, curator of the Phillips Gallery in Washington. Most are of outstanding quality as art, he said. To the psychiatrist, each tells a story of the man or woman who painted it, but little of this reflection of emotional turmoil or progress toward recovery is apparent to others. Mostly oils and water colors, the paintings range in subject matter from a portrait of President Eisenhower to still life of flowers and fruit, outdoor scenes, and abstractions.

Painting is used as an aid in the treatment of mental patients at many VA hospitals, as it gives them a simple means of self-expression with consequent release from tensions. To all appearances, the hospital art clinics are easygoing, pleasant hobby rooms, but beneath the surface there is a great deal of planning and control by the medical staff. Patients are allowed to come in, sit down, and draw or paint at such times as they wish, and to choose their own subject, style of painting, and colors. Instructors are there to help and encourage. The doctors are interested not only in the progress of the patient in the task of painting a picture but in the clues they can get from it as to how he is improving and what is going on in his mind.

Personal.—Dr. Ernest M. Tapp, manager of the Veterans Administration hospital at Dearborn, Mich., since July, 1957, will return to the VA hospital at Poplar Bluff, Mo., in the dual role of manager of the hospital and director of professional services. Dr. Tapp was manager of the Poplar Bluff VA hospital from October, 1952, to June, 1957.

PUBLIC HEALTH SERVICE

Scientists Visit Russia.—Five United States scientists left Washington on May 10 to spend a month in the Soviet Union surveying developments in endocrinology. The mission was sponsored by the National Institute of Arthritis and Metabolic Diseases and was arranged in accordance with a January, 1958, agreement between the two countries to exchange missions in scientific fields. A Russian team of three endocrinologists spent a month this spring visiting American research institutions for the same purpose. Members of the United States team were Drs. DeWitt Stetten Jr. and J. E. Rall, both of the National Institute of Arthritis and Metabolic Diseases in Bethesda, Md., and Drs. Dwight J. Ingle, Ben May Laboratory of the University of Chicago; Rachmiel Levine, of Michael Reese Hospital and the University of Chicago; and Edwin B. Astwood, of the New England Medical Center and Tufts Medical School, Boston.

MEDICAL NEWS

CALIFORNIA

Dr. Bogen to Visit India.—Dr. Emil Bogen is retiring as head pathologist and director of laboratories and research at the Olive View Sanatorium, the tuberculosis sanatorium of Los Angeles County, where he has served since 1929. He was awarded an appointment on the Fulbright Mundt Educational Exchange Program to lecture and carry on research on unusual acid fast bacilli at the Vallabhbhai Patel Chest Institute of the University of Delhi, India, for the nine months beginning in September. His wife, Dr. Jane Skillen, is retiring as a head physician at the Olive View Sanatorium and will accompany him to India. Dr. Bogen was granted leave of absence as clinical professor in the department of infectious diseases in the School of Medicine of the University of California at Los Angeles. He is also on leave of absence as senior consultant in tuberculosis and pathology in the Veterans Administration Hospital in San Fernando.

CONNECTICUT

Annual Hospital Resident-Intern Dinner.—St. Vincent's Hospital, Bridgeport, will hold its annual resident-intern dinner June 24, 7:30 p. m. The evening will be preceded by a day of scientific presentations to be delivered at the hospital nurse's auditorium. Over 25 papers are scheduled for presentation. For information, write Dr. Marvin Garrell, 205 Stillson Road, Fairfield, Conn.

ILLINOIS

Chicago

Dr. Baskind Honored.—Dr. Nathaniel I. Baskind received the annual Gold Medal Award of the Alpha Rho Chapter, Chicago Medical School, of Phi Lambda Kappa, "for service, loyalty and devotion to the School." Dr. Baskind has been a member of the school's board of trustees since 1952 and is chairman of the building committee, directly concerned with the building of the School's new melical research institute.

Society News.—At the annual meeting of the Chicago Dermatological Society Jan. 21, the following officers were elected: president, Dr. Leon Goldman (Cincinnati); vice-president, Dr. Harold Shellow; and secretary-treasurer, Dr. Frederick J. Szymanski.——The newly-elected officers of the Chicago Council of Child Psychiatry are: president, Dr. Anna R. Benjamin; president-elect, Dr. Harry N. Segenreich; secretary-treasurer, Dr. Harold Balikov; and counselors, Drs. Harold A. Greenberg and Jerome Kavka.——At the meeting of the Chicago Urological Society the following officers were elected: president, Dr. Cornelius W. Vermeulen; vice-president, Dr. J. Kenneth Sokol; and secretary-treasurer, Dr. David Presman.——The Chicago Laryngological and Otological Society at their annual meeting elected the following officers for 1959-1960: president, Dr. George H. Woodruff; vice-president, Dr. Linden J. Wallner; and secretary-treasurer, Dr. Robert B. Lewy.

IOWA

Meeting Honors Dr. Langworthy.—The May 12 meeting of the Dubuque County Medical Society in Dubuque honored Dr. Henry G. Langworthy, who served as secretary of the society from 1910 to 1914, and as president in 1941. For many years prior to and following his presidency, Dr. Langworthy was librarian and custodian of the society's records. Guest speaker at the meeting was Dr. Clair M. Kos, professor of otolaryngology, State University of Iowa College of Medicine, Iowa City.

MASSACHUSETTS

Dr. Fawcett Named Department Head.—Dr. Don W. Fawcett was appointed Hersey Professor of Anatomy and head of the department at Harvard University, effective on July 1. Dr. Fawcett has been head of the department of anatomy at Cornell University Medical School since 1955.

MICHIGAN

Hospital Alumni Meeting.—The annual reunion of the Sinai Hospital Alumni Association will be held June 17 in Detroit. The program will include scientific presentations by the house staff, a lecture by Dr. Jacob A. Arlow, visiting chief in psychiatry, and lunch at Sinai Hospital. In the early afternoon, a clinical conference will be conducted by Dr. Arlow. In the evening, a banquet, preceded by a cocktail party at 6:30 p. m., will be held at The Latin Quarter. For information, write Sinai Hospital of Detroit, 6767 W. Outer Drive, Detroit 35, Attention: Assistant Director's Office.

MINNESOTA

British Lecturers.—Dr. Charles V. Harrison, professor of morbid anatomy in the Post Graduate Medical School of the University of London, gave

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Physicians are invited to send to this department items of news of general interest, for example, those relating to society activities, new hospitals, education, and public health. Programs should be received at least three weeks before the date of meeting.

a lecture entitled "Pathology of Pulmonary Hypertension" at the Mayo Clinic, Rochester, May 22, and Dr. Henry Barcroft, professor of physiology in the Sherrington School of Physiology, St. Thomas Hospital, London, England, gave a lecture entitled "The Control of the Circulation in the Limbs" at the Mayo Foundation, Rochester, May 14.

Personal.—Dr. William H. Bickel, head of a section of orthopedic surgery in the Mayo Clinic, Rochester, was elected president of the American Board of Orthopaedic Surgery, Inc., Chicago. He was also reappointed to represent the board on the Advisory Council for Medical Specialties, and is chairman of the residency review committee of the board.——The honorary degree of doctor of humanities was conferred by Nasson College, Springvale, Maine, upon Dr. Charles W. Mayo of the Mayo Clinic, Rochester, Oct. 24. Dr. Mayo was principal speaker at an academic convocation in observance of United Nations Day.

NEW JERSEY

Dr. Bergsma Joins Foundation.—Dr. Daniel Bergsma, state commissioner of health of New Jersey and former president of the Association of State and Territorial Health Officers, was appointed associate director of medical care for the National Foundation, effective July 1. Dr. Bergsma will work with the director of medical care for the National Foundation, Dr. William S. Clark. Dr. Bergsma will share responsibility for formulating new policies of patient aid in the fields of birth defects and arthritis and will direct the foundation's "Operation Softspot," designed to demonstrate techniques for ferreting out big city areas of little or no poliomyelitis vaccination and eliminating them as epidemic hazards by the establishment of neighborhood low-cost clinics. A revolving fund of $500,000 has been set aside by the National Foundation to finance this plan.

NEW YORK

Dr. Greenhill to Give Memorial Lecture.—The Irving W. Potter Memorial Lecture will be given by Dr. Jacob P. Greenhill, professor of gynecology, Cook County Graduate School of Medicine, Chicago, entitled "What's New in Obstetrics and Gynecology," at the annual Homecoming Day of the Millard Fillmore Hospital, Buffalo, June 25. Dr. Greenhill is editor of the "Year Book of Obstetrics and Gynecology."

Society News.—At the annual meeting of the New York Rheumatism Association April 14 the following officers were elected: president, Dr. James A. Coss Jr.; vice-president, Dr. Harry Bartfeld; secretary-treasurer, Dr. Albert W. Grokoest.——Officers for 1959 of the New York Proctologic Society are Drs. Saul Schapiro, president; Maus W. Stearns, vice-president; and Norman L. Freund, secretary-treasurer.

New York City

Dr. Bradley Named Department Chairman.—Dr. Stanley E. Bradley on July 1 will become chairman of the department of medicine, College of Physicians and Surgeons of Columbia University, and director of the Medical Service and an attending physician at the Presbyterian Hospital. He will succeed Dr. Robert F. Loeb who will retire from these posts at the Columbia-Presbyterian Medical Center. Dr. Bradley came to the Columbia-Presbyterian Medical Center in 1947, where he has been associate visiting physician since 1951 and professor of medicine since 1958.

Alumni Association Honors Ex-Presidents.—Twenty-seven M.D.'s were awarded bronze plaques at the annual Alumni Day Celebration of the State University of New York Downstate Medical Center's College of Medicine in Brooklyn May 16. The awards went to all surviving ex-presidents of the 79-year-old alumni association. Nineteen of the doctors graduated from the college between 1897 and 1930, when it was still part of the Long Island College Hospital. The remaining eight received their degrees from the Long Island College of Medicine between 1930 and 1950, before it was merged with the State University of New York to become part of the Downstate Medical Center. Nineteen of the ex-presidents are present faculty members of the College of Medicine.

Personal.—Dr. Robert F. Loeb will retire June 30 as chairman of the department of medicine at Columbia University College of Physicians and Surgeons. Dr. Loeb will also relinquish his post as director of the medical service of Presbyterian Hospital. He will remain Bard Professor of Medicine at Columbia for another year while on sabbatical leave.——Dr. Sidney Rubenfeld, professor of clinical radiology, New York University's College of Medicine, has been named a 1959 recipient of the NYU Alumni Meritorious Service Medallion. A bronze medal with the inscription "To Honor One Who Through Deeds Has Served Alma Mater" was presented to Dr. Rubenfeld at the university's 127th Commencement June 10.——Dr. Harry Gold, professor of clinical pharmacology at Cornell University Medical College, has been elected chairman of the medical advisory board of the Hospital for Joint Diseases.

NORTH CAROLINA

Name Assistant Deans.—Two Duke University School of Medicine professors were named assistant deans of the school. Joseph E. Markee, Ph.D., James B. Duke Professor of Anatomy and chairman of the anatomy department, was appointed assistant dean in charge of admissions. Dr. William M. Nicholson, professor of medicine, was appointed assistant dean in charge of postgraduate education. The new appointments were approved by the executive committee of the university board of trustees.

The third assistant dean in the Medical School is Kenneth E. Penrod, Ph.D., professor of physiology, who will leave Duke this summer to become coordinator of Medical Center affairs at the University of West Virginia. His successor has not been selected.

OHIO

Dr. Dixon Named College President.—Dr. James Payson Dixon Jr., commissioner of public health of Philadelphia since 1952, will become the 15th president of Antioch College, Yellow Springs, on July 1. A 1939 graduate of the liberal arts college, Dr. Dixon succeeds Samuel B. Gould, Antioch president since 1954, who takes over as first chancellor of the University of California at Santa Barbara early in July. Dr. Dixon was a W. K. Kellogg Foundation Fellow in public health administration in 1945-1946, and a Rockefeller Foundation Fellow in 1946-1947. He is a diplomate, American Board of Preventive Medicine and Public Health.

Personal.—The new editor of the *Ohio State Medical Journal* is Dr. Perry R. Ayres, who was appointed to succeed Dr. Jonathan Forman, who resigned.—— Dr. Arthur C. Corcoran, Research Division, The Cleveland Clinic Foundation, presented the Simmons–McBride Lecture to the Faculty of Medicine, University of British Columbia, Vancouver, April 8 on "Clinical Connotations of the Experimental Hypertensions." The lecture was dedicated to the memory of Dr. Eduardo Braun–Menendez, of Buenos Aires.

OREGON

Appropriation for Research Building.—The Oregon State Legislature, in the final days of its 1959 session, passed a $1,297,000 appropriation for the construction of a nine-story research laboratories building on the University of Oregon Medical School Campus, Portland. The appropriation will match an equal sum allocated to the UOMS in September, 1958, by the U. S. Public Health Service through its National Advisory Council on Health Research Facilities Construction. The new building will contain 60,000 square feet of actual research space, according to Dr. David W. E. Baird, Medical School dean. It will contain a radioisotope center, equipment rooms, animal quarters, and scientific instrument shop. Construction will begin early next year with occupancy scheduled for the spring of 1962.

SOUTH DAKOTA

Annual Meeting in Rapid City.—The 78th annual meeting of the South Dakota State Medical Association will be held June 20-23 in Rapid City under the presidency of Dr. A. A. Lampert. The general sessions will be presented under the following symposium titles: Chest Disease, Obstetrics and Gynecology, EENT, Pediatrics, Orthopedics, Genitourinary Problems, and Chronic Fatigue. Out-of-state speakers will include the following: Drs. M. W. Anderson, L. C. Prickman, Elizabeth Mussey, Leonard Aaro, E. H. Rynearson, and Howard R. Rome, Rochester, Minn.; J. B. Gregg, P. J. Leinfelder, and Reuben Flocks, Iowa City; H. Mason Morfit, Denver; Donald C. Nilsson, Omaha; Richard H. Jones, Frederick G. Rosendahl, and T. H. Sweetser, Minneapolis. Luncheon discussions are planned and exhibits are arranged. The dinner dance will be held June 22, 7 p. m. Registration fee is $5. For information write Mr. J. C. Foster, 300 First National Bank Building, Sioux Falls, S. D., Executive Secretary.

TEXAS

Name Research Foundation Director.—Maj. General Elbert DeCoursey, MC, U. S. Army, has been named director of Southwest Foundation for Research and Education, San Antonio. General DeCoursey will also be appointed as a full professor at Trinity University with the title of director of scientific research. General DeCoursey is commandant of the Army Medical Service School and clinical professor of pathology at Baylor College of Medicine, Houston. Southwest Foundation for Research and Education is one of the three independent institutions which make up Southwest Research Center. It is concerned primarily with basic research in medicine. The other institutions in the center are Southwest Research Institute (applied research) and Southwest Agricultural Institute.

WEST VIRGINIA

Residency in Surgery.—A four-year residency program in surgery was approved for the Charleston General Hospital by the Conference Committee on Graduate Training in Surgery, of the American College of Surgeons and the American Board of Surgery. Announcement to this effect was made by the administrator, Mr. A. C. Weaver, who stated that physicians accepted in the future for residencies in surgery, as well as those already in training, will be able to complete their entire residency requirements in the hospital. Previously, the hospital had approval for a three-year residency in surgery.

Personal.—The appointment of Dr. Everett H. Starcher, of Logan, as a member of the Medical Licensing Board was confirmed by the state Senate at an executive session March 14. He had previously been named by Governor Cecil H. Underwood as a member of the board for the term ending June 30, 1963. The Senate also confirmed the appointment of Dr. Margaret T. Ross, of Charleston, as director of the State Department of Mental Health for the unexpired term ending June 30, 1962. She succeeds Dr. William B. Rossman, of Charleston, who resigned to resume private practice in that city.——Dr. Edward A. Litsinger, who has been practicing medicine in Charleston since 1930, has accepted appointment as clinical director of Spencer State Hospital.

WISCONSIN

Dr. Lemmer Honored.—Dr. Kenneth E. Lemmer, professor of surgery, University of Wisconsin Medical School, Madison, was elected to membership in the International Society of Surgery, a world-wide group with its headquarters in Brussels, Belgium. Election to the society is on the basis of research accomplishments. Dr. Lemmer will attend the 18th annual congress of the society in Munich, Germany, Sept. 13-20, as a member of the American delegation. He and the other delegates will be in Austria Sept. 9 and 10 for a series of surgical clinics at the University of Vienna. Dr. Lemmer recently completed his term as president of the Wisconsin Surgical Society.

GENERAL

Board of Anesthesiology Applications.—The American Board of Anesthesiology at its recent meeting voted to consider applications from graduates of Class B medical schools. Those graduates who wish to apply for the board examinations should write to the American Board of Anesthesiology, Inc., 217 Farmington Ave., Hartford 5, Conn., for the proper information and application blanks.

Meeting on Study of Sex.—The Society for the Scientific Study of Sex will hold its second annual meeting Nov. 7 at the Barbizon Plaza Hotel, New York City. There will be two symposiums on the topics "What is Sexually Normal?" and Psychological Factors in Infertility." For details write to Mr. Robert V. Sherwin, Executive Secretary, Suite 704, One E. 42nd St., New York 17.

Sir Robert Muir Dies.—On March 30, Sir Robert Muir, pathologist at Edinburgh, Scotland, died at age 94. After graduating from Edinburgh University in 1888, Sir Robert became a pathologist at the Edinburgh Royal Infirmary and then First Professor of Pathology at St. Andrews University. He later transferred to Glasgow University. Sir Robert was a fellow of the Royal Society for the Advancement of Science. He was knighted in 1934 and received the Lister Medal for his contributions to surgical science.

Portrait of Dr. Bauer.—The headquarters secretariat of the World Medical Association announced that it has received a portrait of oil of Dr. Louis H. Bauer, its Secretary General since 1948. A New York artist was commissioned by the board of directors of the United States Committee, Inc., of the World Medical Association to do the portrait, which was produced without the knowledge of Dr. Bauer. Dr. Austin Smith, chairman of the board of directors, president of the Pharmaceutical Manufacturers Association, and former editor of THE JOURNAL, presented the painting, for display at the secretariat. The inscription on the plaque reads: "Louis H. Bauer, M.D. Presented with appreciation in 1959 by the Board of Directors of the United States Committee of the World Medical Association."

Manual on Adoption of Children.—The American Academy of Pediatrics recently published a 64-page manual on Adoption of Children. Copies can be purchased from the American Academy of Pediatrics, 1801 Hinman Ave., Evanston, Ill., for $1. This manual was prepared by the committee on adoptions under the chairmanship of Dr. Samuel Karelitz, aided by consultants from the Children's Bureau, the Child Welfare League of America, and the International Social Service. It emphasizes the role of the physician, especially the pediatrician, in the adoptive process. Special sections deal with current trends in the adoption of handicapped children, with the problem of intercountry adoption, and the physician's relation to the law. Of special note is an extensive bibliography on many phases of the adoption process.

Medical Director for Dystrophy Associations.—Dr. J. Morrison Brady was appointed medical director of Muscular Dystrophy Associations of America, Inc. Dr. Brady will be in charge of the associations' medical and scientific activities, with responsibility for processing grants-in-aid to research, and for supervising its network of clinics and the other patient services provided through more than 360 chapter affiliates. M. D. A. A. currently supports about 100 research projects in this country and abroad and maintains clinics in 51 major population centers. It has also financed the construction, in New York City, of the Institute for Muscle Disease which is scheduled to begin operations early this summer. Before taking up his new duties, Dr. Brady was affiliated with the National Foundation where he was acting director of medical services and chief of the field medical service division.

Surgeons Plan World Tour.—The International College of Surgeons announced that it will hold its fourth around-the-world postgraduate refresher clinic tour in the late fall. Dr. Edward L. Compere, of Chicago, president of the United States Section, will be the coordinator of medical activities. Departure will be by plane from San Francisco, Oct. 10. The tour participants will take in specially arranged meetings of I. C. S. Sections in Tokyo, Oct. 18-19; Hong Kong, Oct. 29-30; Bangkok, Nov. 2; Tel Aviv, Nov. 20; Istanbul, Nov. 24, and Athens, Nov. 27. Sightseeing trips have been arranged for these and other countries, including Thialand, India, Ceylon, Egypt, Lebanon, and Jordan. Arrival in New York will be about Dec. 1. Accommodations are limited. For information, write to the Secretariat, International College of Surgeons, 1516 Lake Shore Drive, Chicago 10.

Report on Life Expectancy.—Children born this year in the United States have excellent chances of living through the first quarter of the 21st century, according to current mortality conditions as interpreted by statisticians of the Metropolitan Life Insurance Company. In contrast, boys born around

1900 had only two chances in five of living to age 65, while for girls born at that time the chances were only slightly better. For young men of 18 the chances of attaining normal retirement age are about 68 in 100. Somewhat more than 70 out of every 100 men in their late 30's and early 40's can expect to be alive at age 65. Nearly 20% of the men and 30% of the women who attain age 65 can expect to be alive 20 years later. The average future lifetime of white people at age 65, according to current mortality conditions, is nearly 13 years for men, and 15½ years for women.

General Practice Meeting in Oregon.—A northwest regional meeting of the American Academy of General Practice will be held in Portland, Ore., Sept. 9-11 in conjunction with the Sommer Memorial Lectures. All scientific sessions and special luncheons will be held at the College Center at Portland State College. The Sommer Memorial Lecturers are: Drs. Edward H. Rynearson, Leland S. McKittrick, and Howard A. Rusk. Also scheduled to appear are Dr. Richard Eley, Boston; Dr. Leo H. Garland, Stanford Medical School; Dr. Frank W. Norman, Santa Rosa, Calif.; Dr. Ian G. Macdonald, School of Medicine, U. C. L. A.; Dr. Richard H. Overholt, Tufts College; and Roger H. L. Wilson, University of California School of Medicine. A three-day schedule of social and educational events for the wives is also planned. There will be no registration fee. For information, write Mrs. Anna Payne, Executive Secretary, Oregon Academy of General Practice, 4942 N. E. 34th Ave., Portland 11, Ore.

Society News.—At the annual meeting of the **Central Neuropsychiatric Association** March 19-20 the following officers were elected: president, Dr. Harrison S. Evans, Worthington, Ohio; vice-president, Dr. Marvin L. Adland, Rockville, Md.; and secretary-treasurer, Dr. Ralph S. Green, Rochester, Mich.——E. L. Shaffer, Ph.D., 213 Buckingham Ave., Trenton, N. J., was appointed as Executive Secretary of the **American Society of Professional Biologists**, beginning March 1.——The officers of the **American Association for Thoracic Surgery** elected at the 39th annual meeting April 21-23 are: president, Dr. William E. Adams, Chicago; vice-president, Dr. John H. Gibbon Jr., Philadelphia; treasurer, Dr. Julian Johnson, Philadelphia; secretary, Dr. Hiram T. Langston, Chicago; and editor, Dr. Emile F. Holman, San Francisco. The next meeting will be in Miami Beach, Fla., May 11-13, 1960, with headquarters at the Deauville Hotel.

Award in History of Science.—The History of Science Society announced the establishment of a $500 annual award to be given "to an American scholar for a distinguished contribution on a topic related to the history of science." The prize, made possible by Charles Pfizer & Co. Inc., is to be called the Pfizer Award. Selection of the prize winner will be made each year by a rotating committee of three scholars, appointed by the society's president with the approval of its council. Chairman of the committee for this year will be Dr. Owsei Temkin, director of the institute for the History of Medicine at Johns Hopkins University, Baltimore. The intent of the award, according to Henry E. Guerlac, Ph.D., of Cornell University, president of the society, is to supplement the Sarton Medal, given each year to the scholar who in the opinion of the society has made distinguished contributions in the field, and the Schuman Prize for the best essay on the history of science submitted by a student who has not yet earned a doctor's degree. While there are no age restrictions involved in the Pfizer Award, "in practice it will work toward the recognition of postdoctoral scholars without a large body of work to their credit, but who have shown that they are capable of making important contributions."

Foreign Lectureships in Pediatrics.—The Journal of Pediatrics Educational Foundation announced eight foreign lectureships for the week of July 12, preceding the ninth International Pediatric Congress in Montreal. The lecturers (and the medical school where the week will be spent at the department of pediatrics) are:

Dr. S. T. Achar, director, Institute of Child Health, Madras, India (University of Buffalo); Dr. Erkki K. Ahvenainen, pathologist, Regional Medical Center, Jyvaskyla, Finland (Columbia University, New York); Dr. Horst Bickel, professor of pediatrics, University of Marburg, Germany (University of Cincinnati); Dr. K. C. Chaudhuri, director, Institute of Child Health, Calcutta, India (New York University–Bellevue Medical Center, New York); Dr. Wilfrid F. Gaisford, professor of child health, University of Manchester, England (Washington University, St. Louis); Dr. E. Kerpel–Fronius, professor of pediatrics, University of Pecs, Hungary (University of Toronto); Dr. John P. M. Tizard, Institute of Child Health, London (Western Reserve University, Cleveland); Dr. Rolf O. F. Zetterstrom, professor of pediatrics, University of Goteborg, Sweden (Northwestern University, Chicago).

Heart Disease at Middle Life.—A generally downward trend in heart disease mortality rates among persons at middle life in the United States was reported for the eight-year period 1949 through 1956 by the Metropolitan Life Insurance Company's statisticians. This is in contrast to the generally upward trend prior to 1949. The improvement among white males was largely concentrated in the last three years of the period, while among white females the trend was down throughout the period. Heart disease, however, continues to be the most serious health problem among people at ages 45-64 years, accounting for two-fifths of the total mortality and constituting a major cause of sickness and prolonged disability, the statisticians point out. At those ages, the heart disease death rate in the United States during 1955-56 averaged 6.8 per 1,000 among white males and 2.4 among white females. The incidence was about the same in the executive-professional group as in factory and manual workers; and was significantly less than that among clerical workers.

Yugoslavia Gets Rehabilitation Bookshelf.—A contribution to international rehabilitation education was made in Washington, D. C., when, under the auspices of the International Society for the Welfare of Cripples, a "Rehabilitation Bookshelf" was presented to Dr. Ivo Popovic, professor of surgery, University of Belgrade. The presentation was made at the Yugoslavian Embassy in Washington. Rehabilitation Bookshelf is a library of 43 volumes comprising information on rehabilitation. Each bookshelf is "a complete unit of information for doctors, therapists, and laymen." Assisted by voluntary contributions, the international society and CARE are collaborating in assembling and shipping the bookshelf. The project is supported and endorsed by the People-to-People program of the President's Committee on the Employment of the Physically Handicapped. The International Society for the Welfare of Cripples is a federation of voluntary agencies whose programs, carried out in more than 50 countries, deal with the rehabilitation of the physically handicapped.

Air Pollution Meeting in Los Angeles.—The 52nd national meeting of the Air Pollution Control Association will be held June 22-26 at the Statler Hilton Hotel, Los Angeles. About 75 technical papers are scheduled during 15 sessions. Among the topics to be considered are the following:

Health Aspects of Air Pollution.
Problems and Techniques in Air Monitoring.
Radiological Problems in Air Pollution Control.
Atmospheric Contaminant Loadings Throughout the Nation.
Land Use Zoning in Air Pollution.
Control of Motor Vehicle Exhausts.
Source Testing.
Organic Emissions and Air Pollution.
Waste Disposal.

Authors will represent more than 50 organizations including universities, research institutes, consulting firms, private corporations, and air pollution control agencies. A special ladies' program is arranged, and entertainment include tours and the annual banquet. For information write Mr. S. Smith Griswold, Air Pollution Control Association, P. O. Box 54059, Los Angeles 54, Calif., Conference Chairman.

Fellowships for Foreign Students.—Dr. Detlev W. Bronk, president, Rockefeller Institute, announced that the institute received a bequest of about one million dollars from the estate of the late Sophie D. Fricke, of New York City. The trustees of the institute, which was recently transformed into a graduate university, authorized use of the income from the Fricke Fund for the triple purposes of "fostering international understanding, training scientists of exceptional promise, and supporting significant research." Four "distinguished research fellowships" will be awarded each year to young scientists in England, France, Denmark, and Sweden for study and investigation at the institute. The fellows will be appointed by the Royal Society of London, the French Academy of Sciences, the Royal Danish Academy of Sciences and Letters, and the Swedish Royal Academy of Sciences. Each fellow will carry the designation of his sponsoring society. For example, the fellow from England will be known as the Sophie Fricke Royal Society Research Fellow in the Rockefeller Institute. Each fellow will receive an annual stipend of $10,000 with an additional $1,000 for travel in this country. The first fellows will begin their work at the institute this autumn. According to Dr. Bronk, they "will be free to work on problems of their own choosing or they may collaborate with one or more members of the Institute Faculty."

Society News.—The **American College of Obstetricians and Gynecologists** at its seventh annual clinical meeting installed Dr. John I. Brewer, of Chicago, as its president, succeeding Dr. Robert G. Craig, of San Francisco. Dr. Charles P. Hodgkinson, Detroit, was chosen president-elect. Other officers elected are: Dr. Edward C. Hughes, Syracuse, first vice-president; Dr. Ralph W. Jack, Miami, second vice-president; Dr. Axel N. Arneson, St. Louis, treasurer; Dr. Craig W. Muckle, Philadelphia, secretary; Dr. Sprague H. Gardiner, Indianapolis, assistant secretary.——The American **Psychiatric Association** has announced that Dr. Robert H. Felix, Bethesda, Md., is the incoming president-elect of the association, succeeding Dr. William Malamud, New York City, who will become president, succeeding Dr. Francis J. Gerty, of Chicago. Two vice-presidents were elected: Dr. Franklin G. Ebaugh, Denver, and Dr. S. Spafford Ackerly, Louisville, Ky. Dr. C. H. Hardin Branch, Salt Lake City, was reelected secretary, and Dr. Addison M. Duval, Jefferson City, Mo., was elected treasurer.——The **Association of American Physicians and Surgeons** elected the following: Dr. Louis S. Wegryn, Elizabeth, N. J., president, succeeding Dr. Mal Rumph; Drs. William L. Baughn, Anderson, Indiana, secretary; Thomas G. Goldsmith, Greenville, S. C., treasurer; and Thomas L. Dwyer, Mexico, Mo., speaker, House of Delegates.

Fellowships in Rheumatism and Arthritis.—The Arthritis and Rheumatism Foundation offers predoctoral, postdoctoral, and senior investigatorship awards in the fundamental sciences related to arthritis for work beginning July 1, 1960. Deadline for applications is Oct. 31. These awards, intended as fellowships to advance the training of "young men and women of promise" for an investigative or teaching career, are not in the nature of a grant-in-aid in support of a research project. They include:

Predoctoral Fellowships, limited to students who hold a bachelor's degree. Each applicant studying for an advanced degree must be acceptable to the individual under whom the work will be done. Fellowships are tenable for one year, with prospect of renewal. Stipends range from $1,500 to $3,000 per year.

Postdoctoral Fellowships, limited to applicants with the degree of doctor of medicine, doctor of philosophy, or their equivalent. Fellowships are tenable for one year, with prospect of renewal. Stipends range from $4,000 to $6,000 per year.

Senior Investigator Awards, made to candidates holding or eligible for a "faculty rank" and who are sponsored by their institution. Stipends are from $6,000 to $10,000 per year and are tenable for five years.

A sum of $500 will be paid to cover laboratory expenses of postdoctoral fellows and senior investigators. An equal sum will be paid to cover the tuition expenses or laboratory expenses of each predoctoral fellow. For information and application, address the Medical Director, Arthritis and Rheumatism Foundation, 10 Columbus Circle, New York 19.

Rehabilitation Fellowship for Mexican Physician.—The creation of the Smith Kline & French Fellowship in Physical Medicine and Rehabilitation for a Mexican physician to undertake postgraduate training in the United States was announced simultaneously in Mexico City by the Ambassador of the United States to Mexico, the Hon. Robert C. Hill, and Mr. Romulo O'Farrill, president of the Mexican Rehabilitation Association, and in New York City, by Dr. Howard A. Rusk, president, World Rehabilitation Fund, Inc. The fellowship will provide a three-year period of training in physical medicine and rehabilitation for a physician from Mexico. Ambassador Hill announced that Dr. Leobardo Ruiz, of Mexico City, has been selected by the World Rehabilitation Fund as the Smith Kline & French Fellow. Dr. Ruiz will begin his three-year training program at the Institute of Physical Medicine and Rehabilitation, New York University–Bellevue Medical Center, July 1. The fellowship will be administered by the fund in cooperation with the International Society for the Welfare of Cripples. The latter's affiliate in Mexico is the Mexican Rehabilitation Association. The World Rehabilitation Fund is a nonprofit organization supported by American industry, foundations, and individuals to assist in the international development of rehabilitation services for the physically handicapped. Currently there are 71 trainees (57 physicians and 14 nonphysicians) from 35 nations who receive long-term advanced training in the U. S. under the auspices of the fund.

Society News.—The following officers of the **American Association for Cleft Palate Rehabilitation** were elected for 1959-1960: president, Dr. J. J. Longacre, Cincinnati; president-elect, Samuel Pruzansky, D.D.S, Chicago; vice-president, Arthur F. Lindquist, D.D.S., Kansas City, Mo.; past-president, Jack Matthews, Ph.D., Pittsburgh; secretary-treasurer, D. C. Spriestersbach, Ph.D., Iowa City; and editor, Ernest H. Hixon, D.D.S., Iowa City.—At the annual meeting of the **American Urological Association, Inc.,** the following officers were elected to serve for the coming year: president, Dr. William M. Coppridge, Durham, N. C.; president-elect, Dr. John E. Heslin, Albany, N. Y.; secretary, Dr. Samuel L. Raines, 188 S. Bellevue Blvd., Memphis, Tenn.; treasurer, Dr. Grayson L. Carroll, St. Louis; and historian, Dr. Wirt B. Dakin, Los Angeles. The 1960 meeting will be held at the Palmer House, Chicago, May 16-19.—At its meeting April 27-28, the **Society of Neurological Surgeons** elected Dr. Paul C. Bucy, Chicago, president; Dr. Eric Oldberg, Chicago, vice-president; and Dr. Guy L. Odom, Durham, N. C., secretary-treasurer. The next meeting of the society will be held in Seattle in the autumn of 1960.—At the annual meeting of the **American Psychosomatic Society** the following persons took office: Drs. Eric D. Wittkower, Montreal, president; Morton F. Reiser, Washington, D. C., president-elect; and Eugene Meyer, Baltimore, secretary-treasurer. The 17th annual meeting will be held on March 26-27, 1960, in Montreal, Canada.

Prevalence of Poliomyelitis.—According to the National Office of Vital Statistics, the following number of reported cases of poliomyelitis occurred in the United States, its territories and possessions in the weeks ended as indicated:

	May 16, 1959		May 17 1958
Area	Paralytic Type	Total Cases	Total
New England States			
Maine	..	..	..
New Hampshire	..	..	..
Vermont	..	..	..
Massachusetts	..	..	..
Rhode Island	..	..	..
Connecticut	..	..	..
Middle Atlantic States			
New York	..	..	1
New Jersey	2	4	1
Pennsylvania	..	..	..
East North Central States			
Ohio	..	1	..
Indiana	..	2	..
Illinois	..	..	1
Michigan	..	1	1
Wisconsin	1	1	..
West North Central States			
Minnesota	..	..	..
Iowa	1	1	..
Missouri	..	..	..
North Dakota	..	..	..
South Dakota	..	..	..
Nebraska	2	2	..
Kansas	..	2	..
South Atlantic States			
Delaware	..	..	..
Maryland	..	..	..
District of Columbia	..	1	1
Virginia	..	..	..
West Virginia	..	..	1
North Carolina	..	..	..
South Carolina	..	..	..
Georgia	..	..	..
Florida	2	4	4
East South Central States			
Kentucky	..	1	1
Tennessee	..	1	..
Alabama	..	..	..
Mississippi	..	1	1
West South Central States			
Arkansas	2	2	..
Louisiana	..	..	..
Oklahoma	..	..	..
Texas	4	9	5
Mountain States			
Montana	..	..	1
Idaho	..	..	..
Wyoming	..	..	..
Colorado	..	..	..
New Mexico	..	..	..
Arizona	..	..	3
Utah	..	..	1
Nevada	..	..	1
Pacific States			
Washington	..	..	..
Oregon	1	2	..
California	3	3	2
Alaska	..	..	..
Hawaii	..	..	3
Puerto Rico	..	..	6
Total	18	38	34

Students Cited for Exhibits.—At the National Science Fair in Hartford, Conn., May 6-9, the American Medical Association presented four citations to the students judged to have the best exhibits in the basic medical science and health. The citations were awarded at a special A. M. A. banquet, at which Dr. Louis M. Orr (right), A. M. A. president, spoke to an audience of 1,000 students, counselors and teachers from 48 states, the District of Columbia, Germany, Japan, Puerto Rico, and Canada. Dr. Stanley P. Reimann (left), chairman, A. M. A. Council on Scientific Assembly, made the presentation to (left to right) Martin J. Murphy Jr., Colorado, Colo.; Edith K. Schuele, Memphis, Tenn.; Marc W. Deitch (honorable mention), Jersey City, N. J., and Jo Ann Charters (honorable mention), Bay City, Mich. The two first place winners exhibited their studies at the annual meeting in Atlantic City in the scientific exhibit.

Request Applications for Heart Research.—Applications are being accepted by the American Heart Association for support of research to be conducted during the fiscal year beginning July 1, 1960. Sept. 15 is the deadline for applying for research fellowships and established investigatorships. Applications for grants-in-aid must be made by Nov. 1. Support is given not only to studies with a direct bearing on problems of cardiovascular medicine but also to basic research in a wide range of scientific disciplines. The association recently announced its national awards for the 1959-60 fiscal year, representing an allocation of about $3,300,000. Categories in which applications may be made are:

Established Investigatorships: Awarded for up to five years ranging from $6,500 to $8,500 yearly plus dependency allowances, to "scientists of proven ability who have developed in their research careers to the point where they are independent investigators." In addition, a grant of $500 is made to the investigator's department.

Advanced Research Fellowships: Awarded for one or two years to postdoctoral applicants with some research training and experience but who are not clearly qualified to conduct independent research. During the second year of tenure they will be permitted to spend up to 25% of their time in professional and scientific activities not strictly of a research nature, provided that these will contribute to their professional development and do not involve services for a fee. Stipends range from $4,600 to $6,500 annually. Additionally, a grant of $500 is made to the investigator's department.

Research Fellowships: A limited number of awards are available to young persons with doctoral degrees for periods of one or two years to enable them to train as investigators under experienced supervision. Annual stipends range from $3,800 to $5,700.

Grants-in-Aid: Made to experienced investigators to help underwrite the costs of specified projects, such as equipment, technical assistance, and supplies.

Information and application forms may be obtained from the Assistant Medical Director for Research, American Heart Association, 44 E. 23rd St., New York 10.

LATIN AMERICA

Colombian University Expands Medical Research.—The Faculty of Medicine of the University of Valle will enlarge its research programs with the aid of a $125,000 grant from the Rockefeller Foundation. Located in Cali, Colombia, the university will use the funds for the support of researches in biochemistry, obstetrics and gynecology, and endocrinology and hematology, over a period of about three and one-half years. The studies in biochemistry are being led by Dr. Antonio Colas, trained at the University of Edinburgh, who since his appointment as professor of biochemistry at Valle in 1957 has developed a teaching program in the field and formed an interdisciplinary research team for studies on steroids and enzyme systems. Dr. Alvaro Cuadros, leader of the obstetrical and gynecological studies, is emphasizing research on toxemias in pregnancy and on uterine physiology. The relation of the endocrine system to nutrition is the major focus of the researches in endocrinology directed by Dr. Eduardo Gaitan, while the causes of anemia and other hematological conditions will be investigated under the hematology program guided by Dr. Jacobo Ghitis. Founded in 1950, the Cali Faculty of Medicine is inaugurating a program of medical education and care adapted to Colombian cultural patterns.

FOREIGN

University of Louvain Expands Cytology Research.—Continuing support of research in biochemistry under the direction of Prof. Christian de Duve of the University of Louvain, Belgium, The Rockefeller Foundation has appropriated $60,000 for use over a four-year period. In their cytological studies, Professor de Duve and his associates have contributed in the last 10 years to methods of cell particle fractionation. The Laboratory of Physiological Chemistry is now being enlarged. The present grant will be used, like earlier foundation grants dating from 1950, to add to the staff and equipment required for the work of Professor de Duve's program.

Symposium on Radioactive Isotopes.—The fourth International Symposium on "Radioactive Isotopes in Clinical Medicine and Research" will take place in Bad Gastein, Austria, Jan. 7-10, 1960. The topics selected for discussion will be:

Calcium and Strontium Isotopes in the Study of Calcium Metabolism and the Localization of Bone Tumors.
Peripheral Metabolism of Thyroid Hormones and Iodinated Amino Acids.
Radioisotopes in the Study of Glucose and Insulin Metabolism in Normal and Diabetic Patients.
Estimation of Total Body and Extracellular Water.
Estimation of Body Content and Turnover of Electrolytes.
Studies of Red Cell Sequestration by In Vivo Counting.
Estimation of Organ Blood Flow Using Inert Gas Techniques.
New Developments in Radioisotope Therapy.

The official languages will be English, French, and German. Those who wish to present papers should submit abstracts before the end of June to Dr. R. Höfer, Radioisotopes Laboratory, 2nd Medical University Clinic, Garnisongasse 13, Vienna 9, Austria.

EXAMINATIONS AND LICENSURE

NATIONAL BOARD OF MEDICAL EXAMINERS

National Board of Medical Examiners: Various Centers: Part I only, Sept. 9-10. Examinations must be received at least six weeks in advance of a specific examination date. Examining centers established after close of registration. Exec. Sec., Dr. John P. Hubbard, 133 South 36th St., Philadelphia 4.

EDUCATIONAL COUNCIL FOR FOREIGN MEDICAL GRADUATES, INC.

Educational Council for Foreign Medical Graduates: Stations around the world, Sept. 22. Final date for filing applications is June 22. Exec. Director, Dr. Dean F. Smiley, 1710 Orrington Ave., Evanston, Ill.

BOARDS OF MEDICAL EXAMINERS

ALASKA:* On application in Anchorage or Fairbanks. Sec., Dr. W. M. Whitehead, 172 South Franklin St., Juneau.

ARIZONA:* *Reciprocity.* Phoenix, July 15-17. Exec. Sec., Mr. Robert Carpenter, 826 Security Bldg., Phoenix.

CALIFORNIA: *Written.* Los Angeles, Aug. 17-20; Sacramento, October 19-22. *Oral.* Los Angeles, August 15; San Francisco, November 14. *Oral and Clinical.* Los Angeles, August 16; San Francisco, Nov. 15. Sec., Dr. Louis E. Jones, Room 536, 1020 N Street, Sacramento.

COLORADO:* *Examination. Reciprocity.* Denver, July 14. Sec., Dr. John B. Farley, 712 Republic Bldg., Denver 2.

CONNECTICUT:* *Examination.* Hartford, July 14-16. Sec., Dr. Staley B. Weld, 160 St. Ronan St., New Haven.

DELAWARE: *Examination.* Dover, July 14-16. *Endorsement.* Dover, July 23. Sec., Dr. Joseph S. McDaniel, Professional Bldg., Dover.

FLORIDA:* *Examination.* Miami Beach, June 21-23. Sec., Dr. Homer L. Pearson, 901 N.W. 17th St., Miami 36.

GUAM: *Subject to Call.* Act. Sec., Dr. F. L. Conklin, Agana.

HAWAII: *Written.* Honolulu, July 13-14. Sec., Dr. I. L. Tilden, 1020 Kapiolani St., Honolulu.

IDAHO: *Examination and Endorsement.* Boise, July 13. Exec. Sec., Mr. Armand L. Bird, 364 Sonna Bldg., Boise.

ILLINOIS: *Examination.* Chicago, July 7-10. *Reciprocity.* Chicago, July 10. Supt. of Registration, Mr. Frederic B. Selcke, Capitol Building, Springfield.

INDIANA: *Examination.* Indianapolis, June 17-19. Exec. Sec., Miss Ruth V. Kirk, 538 K. of P. Bldg., Indianapolis.

KANSAS:* *Examination and Endorsement.* Kansas City, June. Sec., Dr. F. J. Nash, New Brotherhood Bldg., Kansas City.

MAINE: *Examination and Reciprocity.* Augusta, July 14-16. Sec., Dr. Stephen A. Cobb, Sanford.

MISSISSIPPI: *Examination and Reciprocity.* Jackson, June 22-24. Sec., Dr. A. L. Gray, Old Capitol, Jackson 13.

MONTANA: *Examination and Reciprocity.* Helena, Oct. 6. Sec., Dr. Thomas L. Hawkins, 555 Fuller Ave., Helena.

NEW HAMPSHIRE: *Examination and Reciprocity.* Concord, Sept. 9-12. Sec., Dr. Edward W. Colby, 107 State House, Concord.

NEW JERSEY: *Examination.* Trenton, June 16-18. Sec., Dr. Royal A. Schaaf, 28 West State St., Trenton 8.

NEW YORK: *Examination.* New York, Rochester, Syracuse, Buffalo and Albany, June 23-26. Sec., Dr. Stiles D. Ezell, 23 S. Pearl St., Albany.

NORTH DAKOTA: *Examination and Reciprocity.* Grand Forks, July 8-11. Sec., Dr. C. J. Glaspel, Box 228, Grafton.

OHIO: *Examination.* Columbus, June 18-20. Sec., Dr. H. M. Platter, 21 West Broad St., Columbus 15.

OREGON:* *Examination.* Portland, July 7-9. *Reciprocity and Endorsement.* Portland, July 9-11. Exec. Sec., Mr. Howard I. Bobbitt, 609 Failing Bldg., Portland.

PENNSYLVANIA: *Examination and Endorsement.* Philadelphia and Pittsburgh, July 1-3. Sec., Mrs. Margaret G. Steiner, Box 911 Harrisburg.

PUERTO RICO: *Examination.* San Juan, Sept. 8. Sec., Dr. Joaquin Mercado Cruz, Box 9156, Santurce.

RHODE ISLAND:* *Examination and Endorsement.* Providence, July 2-3. Administrator, Mr. Thomas B. Casey, 366 State Office Bldg., Providence.

SOUTH CAROLINA: *Examination.* Columbia, June 23-24. Sec., Dr. H. E. Jervey, Jr., 1829 Blanding St., Columbia.

SOUTH DAKOTA:* *Examination.* Sioux Falls, Aug. 25-26. Exec. Sec., Mr. John C. Foster, 300 First National Bank Bldg., Sioux Falls.

TENNESSEE:* *Examination.* Memphis, June 17-18. Sec., Dr. H. W. Qualls, 1635 Exchange Bldg., Memphis 3.

TEXAS:* *Examination and Reciprocity.* Fort Worth, June 22-24. Sec., Dr. M. H. Crabb, 1714 Medical Arts Bldg., Fort Worth 2.

UTAH: *Examination and Reciprocity.* Salt Lake City, July 8-10. Dir., Mr. Frank E. Lees, 324 State Capitol Bldg., Salt Lake City 1.

VERMONT: *Examination.* Burlington, June 18-20. Sec., Dr. F. J. Lawliss, Richford.

VIRGINIA: *Examination.* Richmond, June 18-20. *Endorsement.* Richmond, June 17. Address: Board of Medical Examiners, 631 First St., S. W., Roanoke.

WASHINGTON:* *Examination.* Seattle, July 13-15. Administrator, Mr. Thomas A. Carter, Capitol Bldg., Olympia.

WEST VIRGINIA: *Examination.* Charleston, July 13-15. *Reciprocity and Endorsement,* July 13. Sec., Dr. Newman H. Syer, State Office Bldg., No. 3, Charleston 5.

WISCONSIN:* *Written.* Milwaukee, July 14-16. *Reciprocity.* Milwaukee, July 15. Sec., Dr. Thomas W. Tormey, Jr., 1140 State Office Bldg., Madison.

BOARDS OF EXAMINERS IN THE BASIC SCIENCES

ARIZONA: *Examination.* Tucson, June 16. Sec., Mr. Herman E. Bateman, University of Arizona, Tucson.

IOWA: *Examination.* Des Moines, July 14. Sec., Dr. Elmer W. Hertel, Waverly.

OKLAHOMA: *Examination.* Oklahoma City, Sept. 25-26. Exec. Sec., Mrs. L. Haidek, 813 Braniff Bldg., Oklahoma City.

TENNESSEE: *Examination.* Memphis, June 30-July 1. Sec., Dr. O. W. Hyman, 62 South Dunlap St., Memphis 3.

WASHINGTON: *Examination.* Seattle, July 8-9. Sec., Mr. Thomas A. Carter, Capitol Bldg., Olympia.

WISCONSIN: *Examination.* Milwaukee, June 6. Madison, Sept. 11. Sec., Dr. W. H. Barber, 621 Ransom St., Ripon.

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*Basic Science Certificate required.

DEATHS

Bowcock, Harold Mathew Ⓜ St. Petersburg, Fla.; Johns Hopkins University School of Medicine, 1919; retired from the Veterans Administration Nov. 18, 1953; died in the Veterans Administration Hospital, Tuscaloosa, Ala., Feb. 18, aged 64.

Brachvogel, Max William, Aberdeen, Wash.; University of Illinois College of Medicine, Chicago, 1914; veteran of World War I; president of the Acme Door Company and of the Stevenson Plywood Corporation; for many years associated with Grays Harbor Community Hospital; died Feb. 28, aged 68.

Brown, Arthur Granison Boss, Bosworth, Mo.; St. Louis University School of Medicine, 1903; died in Carrollton Feb. 24, aged 86.

Burleson, John Hill Ⓜ San Antonio, Texas; Missouri Medical College, St. Louis, 1890; specialist certified by the American Board of Ophthalmology; fellow of the American College of Surgeons; past-president of the Texas State Medical Association, Bexar County Medical Society, and the Texas Society of Ophthalmology and Otolaryngology; associated with Robert B. Green Memorial Hospital, Baptist Memorial Hospital, Nix Memorial Hospital, and Santa Rosa Hospital; died March 8, aged 91.

Burns, John Gillett Ⓜ Cuero, Texas; Johns Hopkins University School of Medicine, Baltimore, 1920; interned at St. Vincent's Charity Hospital in Cleveland; formerly a resident in general surgery, Mayo Foundation, Rochester, Minn.; fellow of the American College of Surgeons; on the staff of the Burns Hospital, where he died March 9, aged 64.

Byrne, James Whitefield, Brooklyn; Albany (N. Y.) Medical College, 1910; died Feb. 24, aged 72.

Carroll, William James Ⓜ Middleton, Mass.; Tufts College Medical School, Boston, 1935; member of the American College of Chest Physicians and the American Trudeau Society; affiliated with Bon Secours Hospital in Methuen, Lawrence General Hospital in Lawrence, and the Essex County Tuberculosis Hospital; died March 27, aged 56.

Castle, Claude Henry, Los Angeles; University Medical College of Kansas City, Mo., 1903; died March 24, aged 79.

Child, Frank Samuel Ⓜ Port Jefferson, N. Y.; born in Leonardsville, Jan. 3, 1882; Columbia University College of Physicians and Surgeons, New York City, 1909; veteran of World War I; fellow of the American College of Surgeons; past-president of the Suffolk County Tuberculosis and Public Health Association; given the Theodore Roosevelt Award by the Nassau–Suffolk Hospital Council for outstanding service in 1958; mayor of Belle Terre from 1939 to 1958 and village trustee from 1931 to 1939; affiliated with Southside Hospital, Bay Shore, Central Suffolk Hospital in Riverhead, and Eastern Long Island Hospital in Greenport; served as chief surgeon at the Mather Memorial Hospital and the St. Charles Hospital; first president of the Port Jefferson Rotary Club; served as president of the Port Jefferson Literary Association; died at St. Charles Hospital March 23, aged 77.

Chumley, Chonner Polk Ⓜ Chickasha, Okla.; University of Oklahoma School of Medicine, Oklahoma City, 1916; served in France during World War I; at one time served on the faculty at the Student Health Center, Oklahoma University in Norman; superintendent of public health of Grady County; formerly on the staff of the Eastern State Hospital in Vinita and the Western State Hospital in Fort Supply; died in the Veterans Administration Hospital March 1, aged 68.

Collins, Alexander Ballard Ⓜ Morgantown, W. Va.; Louisville (Ky.) Medical College, 1906; appointed to membership on the first Monongalia County Board of Education and was reelected to the board for a term of four years; served as mayor of Blacksville; on the staffs of the Monongalia General Hospital and the Vincent Pallotti Hospital, where he died March 12, aged 79.

Cooney, Michael Edward Ⓜ Northampton, Mass.; Yale University School of Medicine, New Haven, Conn., 1906; veteran of World War I; affiliated with Veterans Administration Hospital, Northampton State Hospital, and the Cooley Dickinson Hospital, where he died March 15, aged 76.

Cox, Napoleon Brock, Shinnston, W. Va., Kentucky School of Medicine, Louisville, 1894; University of Louisville (Ky.) Medical Department, 1897; Hospital College of Medicine, Louisville, Ky., 1897; died March 22, aged 92.

Crane, Charles Austin, Canton, Ohio; Jefferson Medical College of Philadelphia, 1897; served on the staff of the Aultman Hospital; died March 21, aged 83.

Curtin, James Golden Ⓜ Houston, Texas; University of Pennsylvania School of Medicine, Philadelphia, 1925; member of the American Academy of General

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Ⓜ Indicates Member of the American Medical Association.

Practice; served overseas during World War I; on the staff of the North Houston Hospital; died March 16, aged 62.

Davis, Bradley Burns Ⓜ Gainesville, Ga.; University of Louisville (Ky.) School of Medicine, 1914; served in France during World War I; a charter member and past-president of the Kiwanis Club; died in the Hall County Hospital March 17, aged 69.

De Mino, Joseph Anthony, Washington, D. C.; College of Physicians and Surgeons, Boston, 1921; veteran of World War I; served on the staff of the National Homeopathic Hospital; died March 11, aged 65.

Doescher, T. Frederick Ⓜ Albany, N. Y.; Albany Medical College, 1906; veteran of World War I; died March 18, aged 75.

Drynan, Arthur Wellesley Jr. Ⓜ Baytown, Texas; Southwestern Medical School of the University of Texas, Dallas, 1950; veteran of World War II; died March 20, aged 40.

DuBois, Walter Lynn Ⓜ Conrad, Mont.; Northwestern University Medical School, Chicago, 1906; for many years on the staff of St. Mary's Hospital; served several terms as a member of the school board; died March 14, aged 78.

Du Toit, Charles Hill, Boston; Harvard Medical School, Boston, 1942; certified by the National Board of Medical Examiners; interned at Massachusetts General Hospital, where he served a residency; veteran of World War II; served on the faculty of his alma mater; associate physician and chief of biochemistry laboratory, Massachusetts General Hospital; died March 25, aged 42.

Egleston, E. Francis, San Francisco; Rush Medical College, Chicago, 1933; interned at Highland Park (Ill.) Hospital, Chicago Memorial Hospital, and the Franklin Hospital; veteran of World War II; died March 15, aged 54.

Evans, Logan Illk, Danbury, Conn.; University of Oklahoma School of Medicine, Oklahoma City, 1916; veteran of World War I; served in the regular Army; for many years associated with Grace Line Steamship Company; died March 21, aged 71.

Fallis, Daniel Ⓜ West Hempstead, N. Y.; University of Virginia Department of Medicine, Charlottesville, 1928; member of the American Academy of General Practice; school physician for the West Hempstead schools; associated with the South Nassau Communities Hospital in Oceanside and the Meadowbrook Hospital in Hempstead; died in the Columbia-Presbyterian Medical Center in New York City March 17, aged 54.

Fisher, Robert Cockburn Ⓜ New York City; Columbia University College of Physicians and Surgeons, New York City, 1922; veteran of World War II; member of the Industrial Medical Association; assistant medical examiner of New York City; for many years assistant physician at the Union Carbide Corporation; consultant physician at St. Vincent's Hospital; died in the James Ewing Hospital March 8, aged 61.

Fleishman, Norman Arthur Ⓜ Muskegon, Mich.; University of Michigan Medical School, Ann Arbor, 1930; fellow of the International College of Surgeons and the American College of Surgeons; president of the Muskegon County Medical Society; veteran of World War II; a member of the North Muskegon Board of Education; associated with Hackley Hospital and the Mercy Hospital; died in the Mayo Clinic, Rochester, Minn., March 30, aged 50.

Foskett, Harold Stevenson Ⓜ Pasco, Wash.; State University of Iowa College of Medicine, Iowa City, 1924; veteran of World Wars I and II; member of the American Academy of General Practice; associated with Our Lady of Lourdes Hospital, where he died March 22, aged 63.

Frantz, Christian James Ⓜ Warren, Pa.; Starling Medical College, Columbus, 1893; incorporator and past-president of the Warren County Dairy Association; served on the board of Warren Burrough Council and Warren School; instrumental in establishing the Warren Emergency Hospital and for many years served on the board; associated with Warren General Hospital; for many years on the board of the Thiel College in Greenville; formerly on the board of Bethesda Orphans Home in Meadville; died March 14, aged 93.

Fresoli, Michael Ⓜ Bethlehem, Pa.; Jefferson Medical College of Philadelphia, 1926; member of the staff of St. Luke's Hospital; died in the Jefferson Hospital, Philadelphia, March 19, aged 57.

Gebhardt, John William, Mount Lebanon, Pa.; Hahnemann Medical College and Hospital of Philadelphia, 1920; first Mount Lebanon schools medical examiner; served on the staff of the Shadyside Hospital in Pittsburgh; died March 20, aged 72.

Gilligan, Walter Washington, New York City; Georgetown University School of Medicine, Washington, D. C., 1934; interned at St. Michael's Hospital in Newark, N. J., and served a residency at Bellevue Hospital; veteran of World War II; member of the staffs of Beth David Hospital and Doctors Hospital, where he died March 21, aged 52.

Giovinco, Joseph Bivona Ⓜ San Francisco; George Washington University School of Medicine, Washington, D. C., 1924; died March 20, aged 64.

Griffith, Harold Moore Ⓜ Johnstown, Pa.; born in Johnstown June 5, 1898; George Washington University School of Medicine, Washington, D. C., 1920; specialist certified by the American Board of Ophthalmology; fellow of the American Academy of Ophthalmology and Otolaryngology; past-president, second vice-president, and secretary-treasurer of the Cambria County Medical Society; served a term as president of Western Pennsylvania Eye, Ear, Nose and Throat Society; veteran of World War I; consultant in Ophthalmology to the Johnstown plants of the Bethlehem Steel Company, the U. S. Steel Company, and the National–U. S. Radiator Company; business manager of the *Medical Comment* from 1926 to 1928; consultant in ophthalmology at the Windber (Pa.) Hospital; in 1943 elected president of the staff of the Conemaugh Valley Memorial Hospital, where he was chief for many years, and where he died March 26, aged 60.

Harsha, James Mercer Ⓜ Lake City, Fla.; Ohio State University College of Medicine, Columbus, 1926; veteran of World War II; associated with Veterans Administration Hospital, where he died March 10, aged 63.

Herrman, Clinton Simon Ⓜ Philadelphia; University of Pennsylvania School of Medicine, Philadelphia, 1919; served as demonstrator of anatomy at Temple University School of Medicine; fellow of the American College of Surgeons; affiliated with St. Joseph's Hospital and the Albert Einstein Medical Center, Northern and Southern division; died at sea aboard the liner Coronia March 22, aged 62, while on a world cruise.

Hodes, Robert, Orlando, Fla.; Chicago College of Medicine and Surgery, 1916; at one time affiliated with Lincoln (Ill.) State School and Colony, and medical rating member of the adjudication division of the Veterans Administration in Columbia, S. C.; veteran of World War II; died March 11, aged 75.

Hunter, Fred Johnston, Gulfport, Fla.; Starling Medical College, Columbus, 1902; died in the Lenox Hill Hospital, New York City, March 17, aged 85.

Hutchens, Delaney M., Kansas City, Mo.; Kansas City (Mo.) Medical College, 1901; also a druggist; died in the Trinity Lutheran Hospital March 6, aged 83.

Line, Homer Earl Ⓜ Chili, Ind.; Fort Wayne College of Medicine, 1905; served two terms as president of the Miami County Medical Society; veteran of World War I; at various times county health officer; on the honorary staff, Dukes–Miami Hospital in Peru; director of the Wabash Valley Bank in Peru; died Feb. 12, aged 76.

Locker, Harry Loy Ⓜ Brownwood, Texas; Fort Worth School of Medicine, Medical Department of Texas Christian University, 1913; past-vice-president of the Texas State Medical Association; served as councilor of the Fourth District Medical Association; on the staff of the Brownwood Memorial Hospital; veteran of World War I; died Feb. 23, aged 77.

Long, Benjamin Leroy, Glen Alpine, N. C.; North Carolina Medical College, Charlotte, 1913; veteran of World War I; on the staff of the Grace Hospital in Morganton; died in the Veterans Administration Hospital, Salisbury, Feb. 28, aged 71.

Long, Rufus Wilfred, Lowell, Mass.; Tufts College Medical School, Boston, 1917; veteran of World War I; died Feb. 28, aged 67.

McGurl, Thomas Joseph Ⓜ Minersville, Pa.; University of Pennsylvania Department of Medicine, Philadelphia, 1904; for many years member and president of the board of education; on the staff of the Good Samaritan Hospital in Pottsville, where he died Feb. 28, aged 78.

McMullen, Edwin Clare Ⓜ Pine Bluff, Ark.; Rush Medical College, Chicago, 1907; specialist certified by the American Board of Pediatrics; member of the American Academy of Pediatrics; past-president of the Arkansas State Pediatric Association; during World War I served as medical examiner for the exemption board and for the draft board during World War II; died March 9, aged 79.

McNeil, Donald Ⓜ Sacramento, Calif.; Harvard Medical School, Boston, 1926; specialist certified by the American Board of Orthopaedic Surgery; member of the American Academy of Orthopaedic Surgeons and the Industrial Medical Association; fellow of the American College of Surgeons; veteran of World War II and received the Bronze Star medal; associated with Sutter Community, Sacramento County, and Mercy hospitals; died in the Stanford University Hospital Feb. 23, aged 61.

Mackey, Edmund Anthony, Buffalo; University of Buffalo School of Medicine, 1921; formerly on the staff of Our Lady of Victory Hospital in Lackawanna, N. Y.; on the staff of the Mercy Hospital, where he died March 22, aged 62.

Metzger, Herman L. Ⓜ Chicago; Universität Heidelberg Medizinische Fakultät, Baden, Germany, 1925; specialist certified by the American Board of Internal Medicine; veteran of World War II; staff member of the Jackson Park, Weiss Memorial, and Michael Reese hospitals; died March 12, aged 57.

Miller, Hal Curtis Ⓜ Atlanta, Ga.; Jefferson Medical College of Philadelphia, 1909; fellow of the American College of Surgeons; on the staffs of the Emory, Georgia Baptist, St. Joseph's, and Crawford W. Long Memorial hospitals; a director of the First Federal Savings and Loan Association and of the Progressive Life Insurance Company; died in St. Joseph's Infirmary Feb. 27, aged 71.

Monteith, George, Eugene, Ore.; Milwaukee Medical College, 1910; veteran of World War I; died Feb. 26, aged 71.

Myers, Elmer Allen, Homestead, Fla.; University of Kansas School of Medicine, Kansas City, Kan., 1911; formerly practiced in Superior, Wis., where he was president of the staff of St. Mary's Hospital and past-president of the Douglas County Medical Society; died Feb. 26, aged 74.

Pennington, William Hollis Ⓜ Lexington, Ky.; born in Louisville Feb. 10, 1904; University of Louisville (Ky.) School of Medicine, 1928; specialist certified by the American Board of Surgery; member of the Southern Surgical Association; fellow of the American College of Surgeons; served as president and vice-president of the Kentucky Surgical Association; veteran of World War II and was awarded the Legion of Merit for exceptionally meritorious conduct in the performance of outstanding services in the Mediterranean Theater of Operations from Nov. 8, 1942, to May 8, 1945; associated with Good Samaritan Hospital and St. Joseph Hospital; on the staff of the Lexington Clinic; died on a cruise to the West Indies Feb. 19, aged 55.

Pope, Fielding Meigs Ⓜ Brownwood, Texas; University of Texas School of Medicine, Galveston, 1920; died in the Memorial Hospital Feb. 13, aged 66.

Power, Castro James, Harrison, Mich.; Detroit College of Medicine, 1907; died Feb. 23, aged 83.

Reede, Edward Hiram Ⓜ Washington, D. C.; Johns Hopkins University School of Medicine, Baltimore, 1902; member of the American Psychoanalytic Association and the American Psychiatric Association; served on the faculty of Howard University College of Medicine and Georgetown University School of Medicine; joint author of "The American Mind in Action"; associated with the Doctors Hospital, where he died March 14, aged 83.

Schnebly, Joseph George, Captain, U. S. Navy, retired, San Diego, Calif.; University of Kansas School of Medicine, Kansas City, Kan., 1927; entered the U. S. Navy on July 8, 1927; veteran of World Wars I and II; in 1947 became assistant medical officer for the 11th Naval District in San Diego and in 1953 senior member of the physical evaluation board at the Naval Hospital; retired in May, 1958; died in the Naval Hospital Feb. 9, aged 60.

Shewman, Eben Benjamin Ⓜ Cincinnati, Ohio; Eclectic Medical Institute, Cincinnati, 1898; served on the faculty of his alma mater where he was dean from 1933 to 1935; and as demonstrator at the College of Physicians and Surgeons, School of Medicine of the University of Illinois; on the honorary staff of Bethesda Hospital; died Feb. 26, aged 82.

Solomon, Leon L. Ⓜ Louisville, Ky.; University of Louisville (Ky.) Medical Department, 1894; served on the faculty of his alma mater; secretary of the Section on Materia Medica, Pharmacy, and Therapeutics, American Medical Association, from 1897 to 1899, when he became chairman; formerly associated with the U. S. Public Health Service; in 1941 was honored by Jewish Hospital for having served on its staff since the hospital founding in 1902; past-president and one of the original trustees of Charles P. Moorman Home for Women, serving on the board from 1925 to 1949; died in the Jewish Hospital Feb. 27, aged 88.

Spencer, Bennie Elsworth Ⓜ Sterlington, La.; Tulane University School of Medicine, New Orleans, 1929; past-president of the Quachita Parish Medical Society; member of the Quachita Parish School Board; vice-president of the Sterlington Bank; died in Los Angeles Feb. 20, aged 53.

Street, George McQueen Ⓜ Vicksburg, Miss.; Columbia University College of Physicians and Surgeons, New York City, 1913; member of the Southeastern Surgical Congress; fellow of the American College of Surgeons; director of the First National Bank; associated with the Mercy Hospital–Street Memorial, where he died Feb. 24, aged 71.

Tisdale, Alfred Dent Ⓜ Monroe, La.; Tulane University School of Medicine, New Orleans, 1920; fellow of the American College of Surgeons; formerly medical superintendent and owner of the Riverside Sanitarium; on the staff of St. Francis Hospital; died March 2, aged 66.

Turner, George Ellsworth Ⓜ Des Moines, Iowa; Loyola University School of Medicine, Chicago, 1917; died Feb. 27, aged 77.

Werth, Stephen Stafford, Chicago; Dearborn Medical College, Chicago, 1905; medical director of the Reliance Life Insurance Company in Park Ridge, Ill.; died in St. Francis Hospital, Evanston, March 1, aged 80.

Whitesides, William Carl, York, S. C.; University of Maryland School of Medicine and College of Physicians and Surgeons, Baltimore, 1914; on the staffs of the Divine Saviour Hospital in York and the York County Hospital in Rock Hill; died in Charlotte Feb. 28, aged 73.

Wiltse, Clarence E. Ⓜ Wood River, Neb.; College of Medical Evangelists, Loma Linda and Los Angeles, 1949; member of the American Academy of General Practice; certified by the National Board of Medical Examiners; served in the medical reserve corps of the U. S. Army from Aug. 3, 1953, to Aug. 3, 1955; died in Grand Island, Neb., Feb. 26, aged 45.

FOREIGN LETTERS

AUSTRIA

Griseofulvin.—At the meeting of the Society of Physicians in Vienna on March 6, Dr. G. Riehl stated that griseofulvin, a preparation obtained from several species of Penicillium, was found to be nontoxic to human beings when taken by mouth and extremely effective against several diseases caused by fungi. The dosage generally used is two 0.25-Gm. tablets four times daily until a clinical cure results. The drug has been used with success against eczema marginatum, trichophytoses barbae and corporis, mycosis nodosa of the legs, mycotic eczema of hand and foot, and onychomycosis. In the latter condition a cure resulted after extraction of nails without local therapy. Nonspecific cutaneous changes in patients with mycotic eczema of the foot and hand were not influenced by administration of the drug.

Choledochoscopy.—At the same meeting Dr. R. Jellinek discussed the intraoperative diagnosis of disturbances of the common bile duct. The overlooking of stones in the bile duct should be prevented, and changes should be detected which may occur as sequelae of cholangiolithiasis. Cholangiography and manometry have not always provided conclusive information. Choledochoscopy is not to be considered as a substitute for these measures, but the combined use of these three methods can reduce diagnostic errors to a minimum.

Splenectomy and Blood Dyscrasias.—At the same meeting Dr. E. E. Reimer reported on a series of 80 patients who had undergone splenectomy. He concluded that in patients with congenital hemolytic anemia splenectomy should be performed even if the anemia is mild and there are signs of intensive hemolytic activity. Patients with acquired hemolytic anemia should first be given large doses of ACTH or cortisone. Splenectomy should be considered only in patients in whom this therapy is ineffective or cannot be carried out. Active participation of the spleen in the hemolysis should be confirmed with the aid of radioactively labeled erythrocytes before splenectomy is performed. Similar circumstances apply to thrombopenic purpura. Permanent success may be obtained only in chronic forms without immunological proof, associated with megakaryocytosis of the bone marrow. An attempt at splenectomy is indicated in patients with panmyelopathies in whom long-continued hormonal therapy and also blood transfusions have proved ineffective.

Patients with recurrent immunogranulocytosis despite hormonal therapy should undergo splenectomy early. Those with splenogenous neutropenia and with blocking of the bone marrow, respectively, such as may occur in Felty's syndrome, venous thrombosis of the spleen, and similar conditions, should be subjected to splenectomy early, provided the diagnosis has been established. Good results may also be obtained with early splenectomy in patients with hepatic cirrhosis associated with enlargement of the spleen and with splenic anemia. An attempt at splenectomy is advisable in patients with purely splenic lymphocytic leukemia. In other patients with leukemia the spleen should be removed only if uncontrollable hemolysis predominates. Isolated disorders of the spleen, such as lymphogranuloma and reticuloendothelial sarcoma, present an additional indication for splenectomy, although it should be remembered that demonstration of isolated involvement is difficult and may be possible only through operation and observation of the postoperative course.

BRAZIL

New Medical Magazine.—The *Jornal Brasileiro de Medicina* started publication in March in Rio de Janeiro. This new medical review will be issued monthly and will publish the papers read before the Academia Nacional de Medicina, the most important medical society in Brazil.

Gynecologic Radium Therapy.—Vaginal tampons soaked with antibiotics were used by Dr. J. A. V. Piedras of Santa Casa of Rio de Janeiro to eliminate the unpleasant odor caused by vaginal tamponage during radium therapy for gynecologic tumors (*Minerva medica*, December, 1958). The conditions necessary to prevent the growth of putrefactive organisms are permanence of the antibiotic in the vagina; low sensitivity to the antibiotic in powder, suppositories, or solution; and easy absorption through the vaginal walls. Sulfonamides were avoided due to the possibility of producing excessive sensitivity. The author placed radium in position and accomplished the tamponage by means of a Corscaden applicator when the cervix was involved and a Campbell applicator in two patients with involvement of the uterine fundus, impregnating the tam-

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The items in these letters are contributed by regular correspondents in the various foreign countries.

pons with 20 Gm. of 0.5 to 1.0% chloramphenicol ointment. The rectum and the bladder were also protected with tampons impregnated with this ointment. Local radium therapy was continued for 100 to 120 hours, the same tampon remaining throughout this period. No odor was detectable on the gauze and no elevation of temperature occurred during the application of radium. Earlier use of penicillin intramuscularly had no effect on the fever or the odor.

Urologic Complications in the Surgery of Cervical Cancer.—J. Medina and co-workers of the São Paulo State University (*Anais Brasileiros de Ginecologia*, vol. 24, 1959) reported a series of 525 consecutive patients with carcinoma of the cervix uteri. Urinary tract complications in these patients were often more serious than the carcinoma itself. Of the entire series 127 were operated on. They were divided as follows: stage 1, 88 patients, or 69.3%; stage 2, 36 patients, or 28.3%; stage 3, 1 patient, or 0.8%; and remaining stump from previous operations, 2 patients, or 1.6%.Two patients developed vesical fistulas, 13 ureterovaginal fistulas, and one a ureterocutaneous fistula. Of the 63 patients in whom a Wertheim-Meigs operation was performed 11 developed fistulas (2 vesical and 9 ureteral), of the 57 on whom a simple Wertheim's operation was performed 5 developed fistulas (all ureteral), and of the 7 on whom a Schauta's or Brunschwig's operation was performed none developed fistulas.

The frequency of ureteral fistulas is thus much greater after the Wertheim-Meigs operation than after the simple Wertheim's because the first operation is more radical and causes greater damage to the ureters. Of the 88 patients with stage 1 carcinoma 6 developed ureteral fistulas, and of the 36 with stage 2 carcinoma 8 developed this complication. The much greater frequency of ureteral fistulas in stage 2 was due to the greater technical difficulty in performing the operation. The average interval between operation and appearance of the ureteral fistulas in the 14 patients was about 16 days. Of two patients with vesicovaginal fistulas one was successfully treated by occlusion through the vagina and the second was not treated. Of the 13 with ureterovaginal fistulas 8 were treated by reimplantation of the ureter in the bladder, 7 with good results; one was successfully treated by ureteral dilatation; one was successfully treated by bilateral implantation of the ureters in the sigmoid colon; and 3 were not treated. The patient with ureterocutaneous fistula was successfully treated by unilateral nephrectomy.

Other complications included hydronephrosis with pyelonephrosis in two patients, bilateral hydronephrosis in five, and anuria in three. The authors concluded that urologic complications after operations for carcinoma of the cervix are severe and may shorten the life of the patient. The severity of these complications is in direct proportion to the radicality of the operation. The damage to the ureters is not limited to fistulas but may include strictures. For the recognition of lesions other than fistulas urography is essential. The frequency of ureteral lesions, with impairment of the kidneys, is much greater than is currently supposed, and this is a valid reason for abandoning the Wertheim-Meigs operation. During the operation extensive dissection of the ureters must be avoided to prevent their adhesion to the pelvic wall. Vesical disturbances occur after radical operations in direct proportion to the damage to bladder innervation. To prevent vesical atony, a serious complication, it is necessary to maintain continuous drainage of the bladder for at least 15 days.

Nonepileptic Convulsions.—P. Vaz de Arruda and co-workers of the São Paulo State University Hospital (*Hospital* 55:169, 1959) reported a series of 15 patients (12 men and 3 women) who had convulsions without epilepsy. The age of these patients was 18 to 48 (average 27) years. Eight were drug addicts, six were schizophrenic, and one was neurotic. In the latter series the convulsions occurred during psychiatric treatment and in the rest during periods of abstinence from the drug to which they were addicted. Four patients had grand mal seizures when subjected to insulin shock therapy.

The authors found no correlation between the glycemic level and the appearance of convulsions. Furthermore various other hypoglycemic drugs could not cause convulsions even when low blood sugar levels were achieved. Four of the patients who had convulsions when injected with insulin were injected with several convulsant drugs routinely used in treating psychiatric patients, but they had no convulsions from these and their electroencephalographic patterns remained unaltered. In addition to convulsions injection of insulin caused urticaria in two, migraine in one, and asthma in one. The authors believed that the convulsions of these patients depended on an allergic factor. The authors concluded that grand mal seizures may represent an insult to the central nervous system, and may therefore occur in nonepileptic patients. Those occurring during the insulin treatment derive rather from a special state of sensitivity to the drug than from the attendant hypoglycemia. Grand mal seizures occurring after the sudden withdrawal of a habit-forming drug represent only one phase of the general withdrawal syndrome.

CHILE

Increase in Accidents.—Dr. Romero and co-workers of the University of Chile published a study of the increase in accidents. From 1943 to 1955 the population of Chile increased by 20.5% but the number of persons injured in traffic accidents increased by 237%, and fatal traffic accidents increased by 350%. On the basis of figures for 1957 Chile had the highest death rate in the world from all forms of accidents, or 86.7 per 100,000 population. Chile also has the highest homicide rate, 19 per 100,000. This figure includes pedestrians killed by motor vehicles. Chile has the second highest death rate from drowning, 9.9 per 100,000 population. Of all traffic accidents 33% are caused by drivers under the influence of alcohol and 25% by excessive speed. Young men between 20 and 24 years of age are the most dangerous drivers. The highest accident rate occurs between midnight and 4 a. m. Of persons killed in traffic accidents 80% have severe cranial lesions discovered at autopsy.

GERMANY

Streptomycin Injuries.—The claim that the damage to the eighth cranial nerve resulting from prolonged administration of streptomycin could be prevented by the concomitant administration of pantothenate was investigated by Kuschinsky and co-workers (*Deutsche med. Wchnschr.* 84:364, 1959). They gave streptomycin subcutaneously and sodium pantothenate twice daily to 26 cats. After 10 to 15 days impaired equilibrium was observed. Vestibular damage was neither prevented nor delayed by the pantothenate.

Prevention of Tuberculosis.—It has been suggested that in children who are specially exposed to the risk of tuberculosis more effective protection may be possible by combined application of BCG vaccination and isoniazid, rather than by vaccination alone. Experience has shown that the immunizing properties of isoniazid-resistant BCG, which supply the resistant mutant, are in no way inferior to the immunizing ability of isoniazid-sensitive BCG. This is an essential condition for the success of a simultaneous administration of isoniazid and BCG vaccine. As the efficacy of a vaccine for preventive inoculation against tuberculosis is primarily a function of the multiplication of BCG organisms in the body, Kikuth and Pothmann (*Deutsche med. Wchnschr.* 84:360, 1959) believed that it would be worth while to test in animals the protective effect achieved, after previous vaccination, by intermittent treatment with isoniazid-sensitive vaccine and isoniazid-resistant vaccine. They found that the immunizing ability of the mutant resistant to isoniazid did not differ from that of sensitive original vaccines, and the immunity obtained with sensitive BCG with simultaneous application of isoniazid definitely depended on the dose of the vaccine.

The degree of protection afforded by vaccination was proportional to the number of BCG organisms massed together by the vaccination. With intermittent treatment the sensitive BCG organisms had better prospects of survival than they had on continuous application of isoniazid. Hence an essential protection by vaccination was achieved, since this depended primarily on the capacity of the BCG organisms to multiply. These findings were based only on animal experiments, the results of which could not be directly applied to human prophylaxis. These experiments require more extensive investigations, the more so since the dose of vaccine used in guinea pigs was comparatively much larger than that usually used in man. Due to their genotypic condition human beings possess a much greater resistance to tuberculosis than do guinea pigs, but the smaller dose of vaccine used in man would make it all the more necessary to resort to intermittent isoniazid administration in simultaneous prophylaxis.

INDIA

Portal Hypertension.—A. K. Basu (*Journal of the Indian Medical Association,* vol. 32, Feb. 1, 1959) reported a series of 34 patients with portal hypertension who were treated surgically. Splenoportal venography was performed on 32. The pattern of extrahepatic obstruction was seen in 12, of chronic splenomegaly with portal hypertension in 11, of intrahepatic obstruction in 6, of suprahepatic obstruction in 2, and of chronic splenomegaly without portal hypertension in 1. Liver function tests gave normal results in 9, moderate liver damage was revealed in 9, and severe liver damage in 14. Splenectomy alone was performed on 16, splenectomy with splenorenal shunt on 11, ligature of hepatic and splenic arteries on 3, portacaval shunt on 1, and ligature of the splenic artery alone on 1. A follow-up study of 26 patients for six months to four years revealed that 21 were doing well, 3 had recurrence of hemorrhage, and 2 had ascites.

Blood studies were repeated in 18 patients and 16 showed improvement from the preoperative findings; 14 of 18 patients in whom liver function tests were repeated showed better function after operation; and liver biopsy studies were repeated in 12 patients, in 6 of whom improvement was noted. Of 12 patients with extrahepatic obstruction this was due to pancreatitis with fibrosis in 4, cavernomatous transformation of veins in 4, portal vein thrombosis in 2, and pancreatic tumor in 2. Among the 11 patients on whom a splenorenal shunt was performed there were no deaths. Hemorrhage recurred in two and nine were doing well when last seen. The patient with portacaval shunt was benefited by operation. In four patients who had hemorrhage, splenectomy was performed and all were doing well when last seen. Surgical treatment gave better results in patients with extrahepatic obstruction than in those with intrahepatic or suprahepatic obstruction.

The intrahepatic obstruction was due to cirrhosis of the liver in all. Two patients had combined intrahepatic and extrahepatic obstruction—one due to a large hyperplastic nodule and cirrhosis and the other due to portal vein thrombosis secondary to advanced cirrhosis. There were two cases of suprahepatic obstruction, one due to polycythemia vera and the other to constrictive pericarditis. Hemorrhage was a more common feature of extrahepatic than of intrahepatic obstruction and was also more severe and sometimes fatal in this group. All the patients with extrahepatic obstruction gave a history of hemorrhage, in two of whom it was fatal, while only 7 of the 18 patients with intrahepatic obstruction had a history of hemorrhage and these were of lesser degree. In contrast to this, ascites was rare in patients with extrahepatic obstruction but it was present in six with intrahepatic obstruction. In 23 patients the liver was moderately or severely damaged. All of these belonged to the intrahepatic obstruction group.

In patients with extrahepatic obstruction, liver function was essentially normal. Splenoportal venography was helpful in planning the requisite operation. Demonstration of collaterals in splenoportal venography is an accurate guide to the presence and degree of portal hypertension. In most patients the portal venous pressure varied between 200 and 400 mm. of saline solution. There were three patients with pressures above this range. There was no definite relation between the incidence of hemorrhage and the degree of portal hypertension. Most of the patients in this series had large spleens with evidence of hypersplenism. Splenectomy was therefore considered essential in almost all of them. Shunt operation was performed in addition in patients with significant hemorrhage. In some patients chronic splenomegaly was associated with secondary hepatic fibrosis, without a history of repeated hemorrhage. The only evidence of portal hypertension in these patients was the enhanced tension measured at operation. In these patients splenectomy alone was performed with good results. The abdominothoracic approach with division of the diaphragm was suitable in all patients.

Acute Circulatory Stress.—K. K. Datey and coworkers (*Indian Journal of Medical Sciences*, vol. 13, January, 1959) studied 14 patients who were recovering from severe congestive cardiac failure but who still showed some evidence of congestive failure to determine the plasma electrolyte levels after acute circulatory stress. Nine healthy subjects served as controls. The congestive cardiac failure followed cor pulmonale in eight patients, mitral disease in four, aortic stenosis in one, and hypertensive heart disease in one. The plasma sodium and potassium values were determined in all and venous pressure and circulation time in nine patients during the resting and fasting period. They were then subjected to acute circulatory stress by administration of 5 Gm. of sodium chloride in 450 ml. of water by mouth followed an hour later by an exercise test. Immediately after the test samples of plasma were collected for estimation of sodium and potassium values in all cases, and venous pressure and circulation time were again measured in the nine patients previously so tested.

The plasma electrolytes did not show any change after the sodium chloride load and exercise test in the controls. The venous pressure showed a slight rise which dropped back to normal and in some even below normal within a minute or two, while the circulation time showed a reduction in all the controls. In patients with cardiac failure the plasma sodium level remained unchanged after the stress and the plasma potassium level showed a rise in four, a fall in one, and no change in nine. Dyspnea occurred in every patient and persisted for about 15 minutes. The venous pressure registered a marked rise which was maintained for over 15 minutes. The circulation time was unchanged in one patient and showed slight variations in the rest.

Control of Epidemics.—The establishment of a regional council of medical experts from India, Pakistan, Burma, and Ceylon for the adoption of coordinated and simultaneous action for the eradication of smallpox, cholera, malaria, and other diseases endemic in these countries was suggested by Dr. I. A. Cockburn, Provincial Health Adviser to East Pakistan. Dr. Cockburn said that action by one country, however comprehensive it might be, could not prove successful unless supplemented by similar control measures in neighboring countries.

Coronary Occlusion.—K. S. Mathur (*Indian Journal of Medical Sciences*, vol. 13, January, 1959) studied hearts from 1,284 autopsies by injection and dissection. Coronary artery occlusions were found in 342 hearts, giving an incidence of 26.6%. Such occlusions were not present in the hearts of persons under 20 years of age. The maximum incidence was found in the age group from 51 to 80. Although the incidence was higher in men, this difference was less marked after the age of 50 years. Of the hearts with occlusions 176 were analyzed to determine which artery was involved and the number of occlusions; 82 hearts or 46.6% had only one occlusion. The same heart often showed old and fresh occlusions. These 176 hearts together had a total of 360 occlusions, 150 of which involved the left descending artery, 85 of which were in the left circumflex, and 125 of which were in the right coronary artery. Of the 342 hearts with occlusions 88 (25.6%) showed no associated myocardial infarct on either gross or histological examination.

Another group of 14 hearts had myocardial infarction without any evidence of coronary occlusion. Of 264 hearts with myocardial infarction 118 were in the anterior wall, 71 in the posterior wall, 69 occupied both anterior and posterior walls, and 6 were confined to the septum. Posterior wall infarction was present in 140 hearts, an incidence of 52.2%. Twenty hearts or 7% of those with infarction had cardiac aneurysm. All of these were in patients from 46 to 80 years of age. Seven hearts showed cardiac rupture. Myocardial infarction was not a necessary corollary of coronary artery occlusion. Practically all the infarcts were confined to the left ventricle.

Serum Amylase Values.—J. C. Sachdev and coworkers (*Indian Journal of Medical Sciences,* vol. 13, January, 1959) stated that the values of serum amylase in normal persons obtained by different workers show a wide variation. Because this value for Indians had not been estimated, the authors determined the serum amylase value in 100 normal healthy medical students ranging in age between 17 and 22 years. The normal value was found to range from 69.5 to 177.0 units. The average value in vegetarians was found to be a little higher than that in nonvegetarians. No correlation was noticed between the surface area and the serum amylase level.

New Oral Antidiabetic Agent.—In the *Indian Journal of Medical Sciences,* for January, 1959, there is a report of 15 patients who had diabetes mellitus who were treated with K386, a new derivative of tolbutamide. Two tablets of 0.5 Gm. each were given three times a day on the first day. The dose was reduced by one tablet on the second and subsequent days until one tablet three times a day was given. The duration of treatment varied from 2 to 13 weeks. Thirteen of the patients were over 40 years of age. The duration of diabetes was less than 2 years in eight and from 2 to 10 years in seven patients. Nine had received insulin for varying periods prior to the trial. Only three had a family history of diabetes. Two had an associated diabetic retinopathy, one had hypertensive retinopathy, one had pulmonary tuberculosis, and four had cataract. Ten showed good results after this treatment and five were considered failures. Of the 10 treated successfully 8 were obese and 2 of average build; 5 put on weight with this treatment, 1 lost weight and in 9 there was no change. All those treated successfully were over 40 years of age and all had received insulin for less than two years or irregularly.

In these patients the glycosuria disappeared or the amount of sugar excreted was less than 5 Gm. a day. Fasting blood sugar levels were restored to normal or near normal and the blood sugar curve, although remaining abnormal, lowered markedly. Of those treated unsuccessfully two were under 40 and three were 40 years of age or over; three were of asthenic build and two average; two had not received insulin at all and the rest had taken it for varying periods. The duration of the disease was from 2 to 10 years. The renal threshold was raised in only one patient. Routine urine and blood examination and liver and kidney function tests gave normal results. No major complications were noticed but two patients developed boils, which subsided without specific treatment, while being given the new drug. The drug was discontinued in four of the successfully treated patients after some time and all developed glycosuria in two or three days, showing an absence of depot action. One patient was not controlled with K386 alone but had good results when it was given in combination with 5 units of insulin when formerly he required 40 units.

Indian Medical Council.—Inaugurating the silver jubilee of the Indian Medical Council at Delhi in February the Prime Minister expressed concern that India was not doing much medical research. Although this might be because of heavy teaching burdens, research is an important means of improving the quality of both teacher and student. Another pressing problem is adequate medical care in the rural areas. Practitioners of all systems have been reluctant to practice in villages. Despite all efforts made, there has been little real improvement under the first and second five-year plans. It was suggested that every medical practitioner be required to spend a couple of years in rural areas before he could set up practice elsewhere. The Indian Medical Council rather than the government should monitor such a plan. The outlook of physicians would thus be widened. Cheaper types of hospitals should be evolved to meet the difficult problem of providing inexpensive but effective service to the villages.

Nephrotic Syndrome in Children.—Ghosal and Chaudhari (*Indian J. Paediat.* 25:131 [Dec.] 1958) studied 45 cases of nephrotic syndrome in children. All patients had marked proteinuria, hypoalbuminemia, hypercholesteremia, edema, and oliguria. Duration of the disease before admission to hospital varied from five days to seven years. The maximum incidence was seen in the second and third years of life. The preponderance of male patients in the second year was remarkable (10 of 11 such patients). Only 10 of the 45 came from fairly well-to-do families. A history of nephrosis in siblings was present in four. The mother of another child gave a history of nephritis in childhood.

History of allergic manifestations was present in three patients (asthma in one, urticaria in one, and eczema in one). Fifteen patients gave a history of fever and cough or cold immediately prior to the onset of edema. Other diseases preceding edema were jaundice in one, skin rash in one, and diarrhea in one. In another edema was noticed seven days after vaccination against smallpox. The onset of edema was insidious in all but three patients who had oliguria. In most it appeared first on the eyelids, but in some it came first in the legs or genitalia, and in one attention was first attracted by swelling of the abdomen. Thirty-one had generalized edema with ascites. Only one was free of edema at the time of admission. Some children had gross ascites with pitting edema of the abdominal wall and prominent veins, and a few had umbilical and inguinal hernias. The liver was palpable in 20. A history of hematuria at the onset could not be elicited in any case. The systolic blood pressure was below 120 mm. Hg in most. Only 5 of 40 had a persistent diastolic blood pressure above 90 mm. Hg. Remissions and exacerbations during the course of illness occurred in most patients without any apparent cause.

Diarrhea was common and did not respond to treatment. The stools during this period revealed the presence of cysts of Giardia intestinalis in five patients while stool culture showed the growth of only Escherichia coli in the others. Infections of the respiratory tract were even more common and often were followed by an increase in edema. Infections of the eyes, the skin of edematous genitalia, and the inguinal region were frequent. Poliomyelitis complicated the disease in two patients, with hematemesis in one and pleural effusion in one. There was only one death, and it was due to cardiac failure. Tuberculin tests were made on 40 patients and gave a positive result in 10. Twenty-two had hemoglobin values of more than 12 Gm.% and 3 had values below 10 Gm.%. The sedimentation rate varied from 20 to 60 mm. per hour in 34 patients and was normal in 2. Throat cultures showed hemolytic streptococci in seven, staphylococci in three, and Streptococcus viridans in the rest. Albuminuria was present in all. Red blood cells were persistently absent from the urine in 18 patients but they showed hyaline and granular casts at times. The rest had red blood cells and hyaline or granular casts. The total blood proteins varied from 2.85 to 7 Gm.%. Serum albumin was consistently low. The alpha-2-globulin fraction was greatly increased but the gamma globulin was low in all. The blood urea level was more than 40 mg.% in 13.

Chemotherapy for Whooping Cough.—V. D. Arora (*Indian Journal of Child Health*, vol. 8, February, 1959) tried different combinations of isoniazid, prednisone, chloramphenicol, and tetracycline on 60 patients with whooping cough. The diagnosis was mainly clinical. The youngest child was 3 months and the oldest 10 years of age. The duration of paroxysmal cough was one to two weeks in 25 and two to three weeks in 35 patients. Smear and culture examination of nasopharyngeal swabs taken in 53 patients showed Hemophilus pertussis in 6. Isoniazid alone was given to 41 patients, 14 were treated with chloramphenicol and tetracycline, and 5 with isoniazid and prednisone; 14 patients were under one year of age and all responded to one form of therapy or another. Best results were obtained with the combination of isoniazid and prednisone. The five who failed to respond to a seven-day treatment with isoniazid responded to prednisone.

Isoniazid alone gave good results in 70.7% as compared with 57% of those treated with the combined antibiotics, although the relief of symptoms took longer to appear with isoniazid. Thus isoniazid seems to have a definite place in the treatment of whooping cough, and even the 12 therapeutic failures showed some improvement with this drug. Three patients did not respond to antibiotic therapy but gave a good response with isoniazid. The combination of prednisone and isoniazid proved even better, as the response appeared earlier. The response to the antibiotics was also fairly good although all the patients were in the paroxysmal stage, in which antibiotics are considered to be ineffective.

Stress in Children.—De Sa and Soonawalla (*Indian Journal of Child Health*, vol. 8, March, 1959) stated that children are usually believed to show a poor response to major operations. To estimate the biological effect of surgical trauma, which is a recognized stressor, the authors studied the absolute eosinophil count in children undergoing major operations. The effects of maternal stress at childbirth on the absolute eosinophil count of the neonate were also studied. In one group eosinophil variation before and 24 hours after operation was studied in 25 children who underwent major operations under general anesthesia. In 10 of these eosinophil counts were also made 2, 4, and 12 hours after operation to determine short-term fluctuations in this value, if any. In the second group of five children the fall in eosinophil concentrations four hours after an intramuscular injection of 25 mg. of ACTH was studied to compare the effects of a known quantity of ACTH on the eosinophil count and the effect of operation.

In the third group consisting of neonates, the eosinophil count was determined immediately after delivery. Of 61 babies 42 were delivered normally and 10 were delivered by cesarean section. There were six forceps deliveries and three breech deliveries. The response of children in the first group to the combined stress of anesthesia and operation was similar to that in adults, contrary to the usual belief. This may have been due to the relatively large adrenal cortex in children in relation to their body weight. The second group constantly showed eosinopenia following administration of ACTH except in one child who had massive ascarideal infestation. In this child the count showed a rise after the injection. In the group of neonates the eosinophil count fell progressively with increasing difficulty in parturition. The highest eosinophil counts were seen in children delivered by elective cesarean section. Those born by uncomplicated breech delivery came next, followed by normal vertex presentation and those born by cesarean section after a trial labor. The lowest counts were seen in babies born by forceps deliveries. Thus in childhood and infancy stress is felt in much the same way as it is by adults.

Cough Remedies.—Konar and Dasgupta (*Journal of the Indian Medical Association*, vol. 32, March 1, 1959) gave paraldehyde intravenously to determine whether it could be used as a safe and reliable method for exciting the cough reflex in man and whether it could be used to assess the antitussive effect of various cough remedies. Different doses of paraldehyde were used in adults who did not suffer from any cardiac or pulmonary disease, and the minimum dose required to excite cough was determined. Then, keeping this dose constant, the effect of different drugs in suppressing the cough was noted. Cough was induced in 94% of the subjects by rapid intravenous administration of 1 ml. of paraldehyde. This percentage became less as the dose of paraldehyde was reduced. The cough remedies used in the investigation failed to suppress the cough produced by the intravenous administration of 0.1 ml. of paraldehyde. Codeine checked the cough in 2 of 10 subjects but morphine entirely failed to suppress the cough reflex. The circulation time after intravenous injection of 0.1 ml. of paraldehyde, without prior administration of a cough remedy, varied between 5 and 12 seconds. Cough remedies in most cases were found to diminish the circulation time.

The intensity of the induced cough was unaltered by the cough remedies in most of the subjects. The effect on the duration of coughing was more significant. This was diminished on 28 occasions, increased on 13, and on 1 it remained the same. The number of bouts of coughing became less on 24 occasions, increased on 15, and remained unchanged on 3 after administration of the cough remedy. A correlation was thus noticed between duration and number of the bouts of coughing; the drug that would reduce the duration of coughing also diminished the number of bouts of coughing. Thus the intravenous administration of paraldehyde was found to be a safe and effective method for inducing a cough, the stimulus being so potent that most cough remedies could not suppress it. The effectiveness of cough remedies can be measured from their action on the duration and number of bouts of coughing. To assess the comparative usefulness of various cough remedies the chemical stimulus for cough reflex should be minimal.

Transaminase and Myocardial Infarction.—According to O. P. Tandon and co-workers (*Journal of the Indian Medical Association*, vol. 32, March 1, 1959) serum glutamic oxalacetic acid–transaminase (SGO-T) is widely distributed in different organs of the body, the myocardium, liver, skeletal tissues, and kidneys being particularly rich in this enzyme. It is released into the blood as a result of necrosis in these tissues. The authors estimated the SGO-T level in acute myocardial infarction to correlate changes in its value with electrocardiographic and clinical findings, and they also compared the values obtained in acute myocardial infarction with those obtained in related clinical conditions. The normal value was first determined in 40 healthy adults by means of paper chromatography and was found to range between 12 and 38 units. Estimations were then made on 12 patients with acute myocardial infarction, 14 with angina pectoris, and 2 with pulmonary infarction. The electrocardiogram in 7 of 12 patients was diagnostic of acute myocardial infarction and the symptoms and clinical course were also typical of this disease. The SGO-T levels in these seven patients showed a typical time curve of myocardial infarction. The level was raised in all patients, the change appearing within a few hours of the onset of infarction, remaining raised for four or five days, and then returning to normal.

The earliest blood sample was obtained in these patients 20 hours after the attack and the peak level was observed between 20 and 36 hours. The maximum peak level recorded in this group was 210 units and minimum peak level was 62 units. The patient with the 210-unit peak level died within 24 hours of the attack. As such changes as an increase in the leukocyte count and sedimentation rate take three or four days to appear, a rise in the SGO-T level is probably the earliest index of acute myocardial damage. The other five patients with clinical diagnoses of acute myocardial infarction had either normal or inconclusive electrocardiograms, but the SGO-T level was raised in all and showed a time curve similar to that seen in the first seven. Their clinical course confirmed the diagnosis of acute myocardial infarction. Of the 14 patients with angina pectoris the SGO-T level was normal in all but 2, in whom it was raised. In both the patients with pulmonary infarction the levels were normal.

Peripheral Vascular Disease.—R. Nigam (*Antiseptic*, vol. 56, February, 1959) stated that thromboangiitis obliterans in its classic form is rare. The common obliterative lesions of the lower extremity are primary and secondary popliteal artery thrombosis, juvenile arteritis, and senile arteritis. Estimation of skin temperature before and after induced vasodilation does not give a correct picture of the circulation in the muscles from which the pain of intermittent claudication arises. Thus patients with intermittent claudication may still have good color of the skin of the toes, while lumbar sympathectomy may enable areas of cutaneous gangrene to heal with persistence of the pain of intermittent claudication. Plethysmography and microplethysmography before and after vasodilation are probably better guides to the state of blood supply of the limb.

Arteriography is the best method as it gives a correct picture of the site and extent of the block. Instead of the usual method of injecting radiopaque medium into a common femoral artery for visualization of the vessels of the limb, the author found it more advantageous to obtain an aortogram as it also includes the aortic bifurcation and the iliac vessels, the sites most commonly involved. The author performed aortography by the translumbar percutaneous route using 50% iodopyracet in 60 patients with no untoward results. The treatment depended on the degree of occlusion. Early cases responded to medical measures. Lumbar sympathectomy helped patients with a high vasomotor index. The anterior extraperitoneal approach gave good exposure. Advanced cases with established gangrene required amputation. In thrombotic lesions of the iliac and femoral arteries direct operative interference gave good results. Thus a thromboendarterectomy or intraluminal removal of the clot might be performed but in most patients thrombosis recurred in the cleared segment.

A more suitable procedure was replacement of the obliterated segment by an autogenous venous graft, a homologous arterial graft, or a nylon prosthesis. A shunt operation bypassing the obliterated segment was better as it avoided damaging the collaterals. The author performed thromboendarterectomy in one patient with the block in the femoropopliteal artery, with fair results and relief of intermittent claudication. The same operation was performed on another patient with the block in the common femoral artery, with temporary relief but requiring amputation at a later stage. Vein graft shunt was performed on two patients with fair results and dacron prostheses were used on two patients whose iliac arteries were involved, with fair results.

ITALY

Hepatic Cirrhosis.—P. R. Nello of the Pathological Institute of the University of Pisa (*Bollettino della Società medico-chirurgica di Pisa,* vol. 26, 1958) studied a series of 89 patients (71 men and 18 women) with hepatic cirrhosis. The average age of the patients was about 50. The causes underlying the hepatic disease were, in order of frequency, infectious diseases (brucellosis, malaria, and syphilis), alcoholism, and dietetic disorders (specially a deficiency of meat). Most of the patients had trouble with protein metabolism. They also had normochromic or hypochromic anemia, hyposecretion of 11-oxysteroids, and a high serum aldosterone level. Liver biopsy specimens revealed that the most severe morbid changes were associated with brucellosis and malaria.

NORWAY

Gastroduodenal Hemorrhage.—Between 1948 and 1952 a total of 215 patients with acute gastroduodenal hemorrhage attributable to peptic ulcer, gastric carcinoma, or gastritis were treated by J. R. Myrhe (*Nord. med.* 61:212-215 [Feb. 5] 1959). In the following five-year period, 1953 to 1957, the corresponding figure was 256. In the first period only 2 patients were operated on, and in the second 23 patients were treated surgically, the operative mortality being 8%. From the first to the second period the total mortality fell from 5.1 to 2.0%, or from 9.5 to 3.3%, if only severe hemorrhages were included. The differences between the results in the first and second period were not statistically significant, but operation was definitely recommended in selected cases.

Essential Hematuria.—Audun Flatmark (*Nord. med.* 61:215-218 [Feb. 5] 1959) made a follow-up examination of 85 patients discharged from the department of surgery, Aker Hospital, Norway, with a diagnosis of hematuria, cause undetermined. In 30 patients certain findings which might be a possible though doubtful cause of the hematuria were recorded during their stay in hospital; 18 of these later became asymptomatic, and it was not presumed that the original findings in these patients were the cause of the bleeding. In the remaining 12 patients other diseases were later diagnosed: 7 had carcinoma of the urinary tract, 3 had renal failure, and 2 had renal stones. Of the 55 patients who were discharged from the hospital without any findings to explain the hematuria, urinary diseases developed later in 22. One patient died of mitral stenosis and congestive heart failure. In the remaining 32 patients no cause of the hematuria was found. The bleeding in these patients might have been caused by small lesions in the kidneys which could not be found unless the kidneys were removed at operation or at autopsy. Renal varices or papillary hemangioma might have been the cause in these patients.

Fracture of the Calcaneus.—Arne Arnesen (*Acta chirurgica scandinavica,* supp. 234, 1958, pp. 1-51) reported on a series of 77 fractures of the calcaneus in 67 patients, 68 of which were through the body of the bone. Tongue-type fractures, depression-type fractures, and stamp-type fractures are universally recognized. In 33 of these patients traction was applied for six weeks. Thereupon exercise therapy was instituted without weight-bearing. Beginning about 12 weeks after the accident weight-bearing was permitted. Follow-up examinations of 58 patients were made. With regard to extra-articular, depression-type, and slight stamp-type fractures good results were achieved anatomically and subjectively by treatment with closed reduction and traction. It was recommended that the indication for active therapy be extended to include also the slight fractures. As far as the severe stamp-type fractures were concerned reduction of the joint fragment was not successful, although the subjective result had been satisfactory.

With regard to tongue-type fractures results of treatment with reduction and traction were not satisfactory, and it was recommended that the joint fragment be reduced by a Gissane spike. In 38 of the total of 58 follow-up examinations good results were found. Forty-two patients recovered a normal gait; 44 returned to their old jobs, 12 to lighter work at the old job, and 2 were unfit for work due to intercurrent disease. The good results were attributed to the fact that by traction a good axis was nearly always obtained and as a rule also good support for the talus, and further that exercise therapy was instituted from the first day.

Rheumatic Heart Disease.—At a meeting of the Bergen Medical Society Prof. Erik Waaler reported rheumatic heart disease in 219 of a series of 5,460 autopsies. In 33% of these the involvement of the valves of the heart was an incidental and unexpected finding. With rheumatic heart disease found in about 4% of all autopsies in Bergen no decline in the incidence of chronic heart disease was demonstrable in the period under review (1941 to 1955); most of the acute cases belonged to the preantibiotic era. The incidence of rheumatic heart disease was twice as high for old women as for old men, but no such sex difference was demonstrable in the younger age groups. By distinguishing between the different age groups in respect to sex the author suggested that he might have found a clue to the contradictory verdicts of earlier observers on the influence of sex on heart disease. He was surprised to find how long had been the mean interval between an attack of rheumatic fever and death. This was 32 years, and the mean age of the patients was 52 years. The author was surprised to find that in elderly women a rheumatic infection often runs a silent, atypical course in comparison with that of elderly men.

Cervical Lymph Node Biopsy.—Between 1953 and 1958 retroclavicular, prescalene, cervical lymph node biopsy was performed on 117 patients at Ullevaal Hospital. Hoel and Sandvig (*The Journal of the Oslo City Hospitals*, vol. 9, January, 1959) reported that positive findings were obtained in 31 and in 8 of these sarcoidosis was identified. In two others the clinical diagnosis of sarcoidosis was not confirmed by the biopsy. Of the 41 patients with bronchogenic carcinoma the biopsy specimens of 15 showed metastases. In none of the nine patients with pulmonary fibrosis did the biopsy reveal any pathological tissue. This negative finding helped to confirm the clinical diagnosis. One of the 117 biopsies performed provoked paralysis of the right phrenic nerve of a woman who became dyspneic. She showed roentgenographic signs of mediastinal flutter and paradoxical respiration on the right side. Her symptoms receded gradually, but four months after the operation movements of the right diaphragm were still reduced. In another patient a fistula developed after the lymphatic duct had been wounded on the right side. Three months later autopsy revealed a lymphatic cyst in the operative scar.

Psychiatric Aspects of Plastic Surgery.—Dr. J. Odegard (*Nordisk medicin*, Jan. 15, 1959) observed psychiatric reactions in eight patients who underwent plastic operations at Ullevaal Hospital in the preceding five years. In a patient with torticollis the plastic operation for it led to complete decompensation of a formerly well-compensated neurosis. In another patient two rhinoplastic operations had yielded excellent cosmetic results, yet the patient pestered and threatened her surgeon in order to have a third operation. A strong element of narcissism is often to be detected in applicants for plastic operations, and it may be that nearly all in this class are psychiatric patients with some irrational background for the wish to benefit from cosmetic surgery.

Prevention of Heart Infarct.—Dr. C. Bjerkelund (*Nordisk medicin*, Jan. 22, 1959) analyzed a series of 237 patients who had been treated for acute myocardial infarction at Ullevaal Hospital and had recovered enough to be discharged. All were under 76 years of age; 119 were put on permanent anticoagulant treatment with bishydroxycoumarin and 118 served as controls. During the six and one-half years of this comparison both groups were kept under systematic heart control. The mean duration of treatment was 52 months. Among the 78 deaths in the two groups only 5 were not traceable to cardiovascular disease. Among the controls there were 21 deaths from recurrence of the infarct, whereas there were only 13 such deaths among the treated patients. The deaths registered as "sudden" numbered 12 and 7, respectively, and those registered as "heart failure" numbered 5 and 2 respectively. On the other hand there were four deaths from cerebral hemorrhage in the treated group as compared with only one such death in the control group. In the former there were 28 patients with infarct recurrence as compared with 43 in the latter, and the total number of recurrences was 34 for the treated group and 52 for the control group. This beneficial effect of bishydroxycoumarin was demonstrable only during the first 12 months of the treatment.

National Campaign for Epileptics.—The first half of March was devoted to an appeal and educational campaign throughout Norway on behalf of the 20,000 epileptics in the country. At a meeting attended by King Olav it was pointed out that about 13,000 were fit for work and were at work. Among the 6,000 unable to get regular work because of their liability to attacks there were many who would profit from prolonged observation and treatment in hospitals specializing in epilepsy. Many of the 177 beds in the State Hospital for Epileptics were taken by patients with chronic cases more suited to nursing homes for the incurable. The remaining 1,000 patients had such gross lesions of the brain with mental deterioration and paralyses that they were also in need of institutional care.

SWEDEN

The Münchhausen Syndrome.—Dr. Bengt Hamrin (*Svenska läkartidningen*, Feb. 27, 1959) reported a case of Münchhausen syndrome in a 38-year-old man. Since 1952 he has gained admission to many hospitals by exercise of his histrionic gifts, supplemented by his mastery of the symptomatic behavior of such diseases as rabies, poliomyelitis with respiration paresis, and tetanus. Simulating rabies on admission to a hospital in Denmark he narrowly escaped undergoing tracheotomy. Later in a Swedish hospital he was actually tracheotomized. What with his tracheotomy scar and the publicity his saga has gained him, the further pursuit of his hospital itinerary must be increasingly difficult. The author pleads for a kindly tolerance of the urge in certain persons to simulate disease in order to enjoy the sympathy of doctors and nurses and the comforts of hospital life.

Guinea Pig Allergy.—Dr. G. Gottfarb (*Svenska läkartidningen*, Feb. 20, 1959) observed five cases of asthma traceable to pet guinea pigs. The first patient was a man, aged 39, who gave positive reactions to skin tests to horse and guinea pig and who had kept a guinea pig in his home for about a year. His nightly attacks of asthma ceased soon after the guinea pig was got rid of, and they had not recurred on reexamination nine months later. Another patient, aged 45, gave his children a guinea pig in the spring of 1958. In the summer of that year he began to suffer from coryza, cough, and dyspnea which became worse when he held the guinea pig on his knee. These symptoms vanished after he had got rid of it. Intracutaneous testing with a 1:100,000 dilution of guinea-pig extract yielded a strong reaction. In all five patients the guinea pigs had been in the patients' homes for some time before symptoms occurred, and in one handling the animal did not at once provoke asthma.

Diuretic Action of Chlorothiazide.—Dr. H. Bucht and co-workers (*Nordisk medicin*, Feb. 12, 1959) used chlorothiazide to treat about 300 patients with heart failure. The toxicity of the drug is low and its therapeutic range is wide. One of its greatest merits is that it can be given by mouth with just as great diuretic effect as that achieved by the parenteral administration of the mercurial diuretics. In patients with slight or moderate cardiac insufficiency the desired effect can be obtained with 500 mg. (one tablet) every second or third day. In more severe cases up to 2 Gm. daily may be given, but then an extra dose of potassium (1 to 3 Gm. of potassium chloride, for example) should be given daily. This treatment has been given continuously or intermittently for up to 11 months, and it has reduced weight in patients with dropsy by up to 10 kg. (22 lb.) in a few weeks. Patients with hypertension without cardiac insufficiency have as a rule responded by a fall in blood pressure without loss of weight. In four patients with acute myocardial infarct, edema of the lungs, and a low blood pressure good diuresis was effected without a change in blood pressure. In only one patient was the drug discontinued on account of gastric disturbance. Erythema developed in one patient and pruritus in two. Patients whose symptoms had become refractory to mercurial diuretics often responded well to chlorothiazide, and in severe cases the two may have to be combined in order to obtain the desired effect. Recipients of this drug should be kept in electrolyte balance. The drug is recommended for outpatient as well as hospital practice.

Proton Radiation for Cancer.—*Svenska Dagbladet* for Feb. 27 contains an account of the work on proton radiation at the Werner Institute and the gynecologic department of the Akademiska Hospital in Uppsala under the auspices of Professors Naeslund and Svedberg. In 1956 Naeslund grafted cancer cells into the ears of rabbits. While the right ears were treated by proton radiation, the left ears served as controls. Another series of rabbits was given roentgen irradiation of the affected ears. It was found that healthy tissues could stand a dose of proton radiation twice as great as the maximum x-ray dose. Experimental cancer of the uterus of rabbits healed under proton radiation without destruction of healthy tissues. Encouraging observations were also made on other organs in the rabbit. In the autumn of 1957 a woman suffering from cancer of the uterus was treated with proton radiation, and while the growths directly exposed to treatment receded the others progressed. Encouraging results were obtained with growths secondary to cancer of the breast in an elderly woman, but this case is too recent to justify drawing any final conclusions.

Memory Disturbances After Electroconvulsive Therapy.—A series of 30 patients were given a battery of memory tests a few days before the first electroshock treatment in a series, and another battery of tests one week after the last electroshock treatment. The two forms of the tests were used alternatively before and after the treatments by Cronholm and Blomquist (*Acta psychiat. et neurol. scandinav.* 34:18-25, 1959). The mean number of treatments was 3.6 over a mean period of 10.1 days. The first battery comprised three memory tests for evaluation of recall immediately after learning and three hours later, called the 30-word–pair test, the 20-figure test, and the story test. Another new test called the 15-letter–symbol-pair test, consisting of paired associates and intended to serve the same purpose, and a vocabulary test were also given. About 45 minutes before treatment the patients received 0.26 mg. of methylscopolamine (Skopyl) nitrate intramuscularly. Immediately before treatment they were given 0.25 to 0.50 Gm. of hexobarbital and 0.2 to 0.7 Gm. of succinylcholineiodide (Celocurin) intravenously. The treatments were usually given twice a week. After the treatments there was a significant decline in the number of items recalled three hours after learning in the word-pair and figure tests. In the word-pair test there was also a significant decline in the score for retention and a significant increase in the items forgotten. In the other tests no significant differences between the performances before and after treatment were found.

Involutional Melancholia.—Åke Stenstedt (*Acta psychiat. et neurol. scandinav.* 34:1-71, supp. 127, 1959), studied a series of 307 patients (70 men and 237 women) with involutional melancholia and their siblings and parents, 2,282 persons in all. One-tenth of the patients had one parent with an endogenous affective disorder, and at least one parent of 34% suffered from severe mental disease. Of the patients themselves 74% had had only one depressive attack; in 45% the personality was considered as deviant; 25% became depressed in connection with a psychic trauma and 36% in connection with some other exogenous factor; in 13% agitation was clearly evidenced, in 20% retardation, and in 10% bizarre, hypochondriacal, negativistic delusions; and 9% of the women had their only depressive attack in connection with the menopause. Childhood environment was considered unfavorable in 33%. The mean age at onset for all patients was 57.5 years, and for all 86 with secondary cases and endogenous affective disorders, 48.2 years. Mania occurred in four of the secondary patients with endogenous affective disorders. No resemblances within the families could be shown for those who had endogenous affective disorders. Among hospitalized patients with involutional melancholia the unmarried and divorced were preponderant.

The patients did not differ from the general population in respect to social class. They had a fairly high death rate. The frequency of suicide among them was higher than in the general population. Women with endogenous affective disorders were hospitalized more often than men. Hereditary factors entered into the etiology of the material, probably especially in the subgroup with one parent who had an endogenous affective disorder but also in the case of patients with agitation. The disease was probably not hereditary in those with symptoms in connection with a psychic trauma, retardation as a main symptom, single depressive attack in connection with the menopause, or advanced age at onset.

Operation on Diabetics.—Kjell Stenberg (*Nord. med.* 61:210-212 [Feb. 2] 1959) reported that the operative mortality for diabetics was still relatively high, about 9%. This figure is notably lower than that recorded 15 to 20 years ago, and this was attributed to more rational insulin therapy, better fluid and electrolyte balance, and treatment with antibiotics. The present series comprised 246 states of anesthesia in 149 surgical patients. Ketonuria occurred in a large number after local and spinal anesthesia. The trauma caused at operation may also have produced acidosis. Those patients who had ketonuria before operation were more likely to develop acidosis postoperatively even after relatively rational insulin therapy. When increased amounts of insulin and carbohydrate were given postoperative ketonuria occurred less often than when reduced or ordinary doses were given on the day of operation. Administration of carbohydrates in increased amounts plus insulin, to patients who had earlier required dietary control alone, should be considered.

On the day of operation the usual morning dose should be given and an adequate supply of carbohydrates be assured by the administration of dextrose. In refractory cases it is advisable to give increased doses of insulin on the day of operation, and these can be given in the form of a dextrose-insulin solution containing one unit of insulin for each 2 Gm. of dextrose. As regards the stabilization of the patient's diabetes the amounts of sugar in the urine should be lowered to about 5 Gm. per 24 hours before operation. For premedication meperidine and atropine were recommended. Because of its high toxicity chloroform is contraindicated in diabetes. The suitability of ether may be questioned, but because of its beneficial effect on the circulation the author believed that it could not be wholly abandoned. Combined anesthesia with muscle relaxants was recommended, although as a general rule it is advisable to use the form of anesthesia with which the anesthetist concerned is most familiar. A review of the causes of death showed that attention should be focused on the patient's circulation.

The author recommended (1) careful preoperative control of the patient's diabetes with respect to ketonuria and glycosuria with a possible changeover to a quick-acting insulin and increased intake of carbohydrate; (2) induction of anesthesia with special consideration of the importance of avoiding a fall in blood pressure and of maintaining adequate oxygenation; (3) administration of insulin in a sufficient amount and, if necessary, an increased supply of carbohydrates in the form of dextrose, with careful checking of the variations in blood sugar level on the day of operation; and (4) intensified postoperative care aimed at preventing respiratory and circulatory disturbances.

Fractures of the Carpal Scaphoid.—Wallensten and co-workers (*Acta chir. scandinav.* 116:148-154, 1958/1959) studied a series of 62 patients with fresh fractures of the carpal scaphoid with the line of the fracture running through the so-called waist or else proximal to it. They were all treated conservatively by immobilization of the wrist and the proximal phalanx of the thumb in a circular plaster cast. Union occurred in all. No pseudarthrosis occurred in spite of several of the patients having circulatory disturbances. At the follow-up investigations 59 patients were found to be free of trouble and the residual symptoms in the others were slight. Comparison with a series in which the thumb was left completely free revealed that by immobilizing the thumb the average time for the complete treatment was reduced by 56 days.

Aneurysms of the Middle Cerebral Artery.—A series of 80 patients with aneurysms of the middle cerebral artery, of whom 76 had ruptures, was reported by Höök and Norlén (*Acta chirurgica scandinavica*, supp. 235, 1958, pp. 1-39). After discharge the patients were followed up for an average of 3.7 years. The average age at the time of admission to the hospital was 42 years and the sex ratio was 1:1. In some patients the hemorrhage was preceded by headache, often of a few years' duration. The first symptom in most of the patients was unconsciousness. In 64 patients the dominant focal neurological sign was hemiplegia or hemiparesis. In those patients in whom the headache was unilateral this symptom provided a good guide to the localization of the aneurysm. Of the patients with ruptured aneurysms two had epileptic seizures before and nine after the hemorrhage. Epilepsy occurred in three of the four patients with unruptured aneurysms. Visual hallucinations were encountered in two patients, in one of them in immediate association with the hemorrhage. Endocrine symptoms were found in two patients. One of them showed symptoms similar to those seen in pituitary basophilism. The other, who had a large aneurysm, had symptoms of hypopituitarism due to destruction of the sella turcica. Thrombosis of a large aneurysm shortly after the hemorrhage was observed in one patient.

Operation was performed on 64 patients. In 45 of them the neck of the aneurysm was ligated. Four of these patients died shortly after the operation; two were in deep coma at operation and two were semiconscious, disoriented, and had severe neurological signs. It would seem that operation in this stage was contraindicated. Operation seemed indicated as soon as a patient had recovered from the immediate consequences of the hemorrhage. Hypertension and advanced age were not per se contraindications for operation. It was impossible to give definite rules, as these cases must be judged individually. Of the group operated on 59 survived the first eight weeks after the hemorrhage which caused admission to the hospital. Of these one died of a recurrent hemorrhage in the follow-up period. Of the 41 who survived operation in which the neck of the aneurysm was ligated, 2 had recurrent hemorrhages and one died. Thirty of them had full working capacity; eight had partial work capacity; and three were total invalids, but the disability was not the result of their operation.

Sympathectomy in Obliterative Arterial Diseases.—A series of 104 patients (88 men and 16 women) with an average age of 53 years who underwent sympathectomy because of claudication with or without pain at night or gangrene were followed up by Argo Kövamees (*Nord. med.* 61:135-138 [Jan. 1] 1959). Sympathectomy was found to be a relatively safe and nondebilitating operation, which the elderly patients tolerated well. Lasting improvement of the claudication was obtained in 46% of the patients. The degree of clinical improvement was compared with the degree of obstruction found arteriographically, and the best results were noted for those who had radiographically demonstrable collateral vessels around the main obstruction. An efficient collateral circulation seemed to be a prerequisite for improvement in walking ability after sympathectomy. Nocturnal pain was greatly relieved even in those patients in whom the operation had no effect on the claudication. Among those in whom claudication before operation was associated with pain at night, walking ability improved in a greater number of patients than it did in those who had only claudication as the main symptom. The explanation of this would presumably be that in the former there was a more markedly spastic condition which was relieved by the operation. A persistent feeling of warmth in the lower limbs occurred in practically all the sympathectomized patients. Pregangrenous or gangrenous changes were only slightly improved by the operation.

UNITED KINGDOM

Metabolism of Myelin.—Some of the earlier work on the turnover of myelin lipids, with radioactive phosphorus (P^{32}), suggested that throughout life the phospholipid components of the myelin sheath are undergoing constant renovation. Doubt was cast on this concept of dynamic metabolism within the myelin sheath by Prof. Payling Wright and co-workers (*Lancet* 1:658, 1959). They injected 5 μc of cholesterol containing radioactive carbon (C^{14}) intraperitoneally into 17 one-day-old rabbits, an age at which myelinization in the central nervous system is proceeding. Animals were killed at roughly equal intervals during one year, and the labeled cholesterol content was estimated from its radioactivity in various parts of the brain, spinal cord, heart, liver, kidneys, and plasma. Segments of sciatic nerve were excised and the cholesterol content estimated.

After a year the labeled cholesterol was found to persist in the central nervous system, although it had disappeared within the first few months from the heart, liver, kidneys, and blood. In the central nervous system the degree of persistence of the labeled cholesterol differed in the gray and white matter. In the former there was evidence of turnover during the first few months, while in the latter there was little indication that this substance, once incorporated, was later lost. The radioactive cholesterol recovered from the brain a year after its injection still retained its C^{14} at the original position in the molecule. It would therefore seem that the myelin lipids may remain indefinitely in the nerve sheaths where they were laid down originally during the development of the central nervous system. These observations may throw some light on the pathogenesis of the demyelinating diseases.

Reporting Unfit Motorists.—A doctor should report a person who is unfit to drive a motor vehicle and who refuses to surrender his license, according to Dr. Francis Camps, Reader in Forensic Medicine, London University. When a patient behaves thus the doctor finds himself bound by secrecy because of his professional relationship. The easiest precaution is to obtain a second authoritative opinion. If the advice not to drive is still refused, the doctor is in some difficulty. Although bound by professional secrecy, he can foresee the injury or death of innocent persons. Bearing in mind that the patient's own interests are involved it is most improbable that any lawsuit would succeed against the doctor, should he reveal his knowledge to the authorities.

Blood Group Symposium.—The May, 1959, issue of the *British Medical Bulletin* is devoted to a symposium on blood groups. Dr. A. E. Mourant served as chairman of the committee which planned the symposium, wrote the introduction, which summarizes the current work in the field, and contributed a paper on blood groups and anthropology. Much of the work described in the 14 papers is recent and a good deal of it was done by British workers who reported on their own research and reviewed important recent contributions from various other countries. Each paper is well documented. Because of the wide ramifications of the subject, this symposium should be of great interest not only to the worker in the special field of blood groups and transfusion but also to the biochemist, immunochemist, immunologist, serologist, geneticist, physical anthropologist, pathologist, pediatrician, obstetrician, biologist, veterinarian, and botanist. The price is $3.25.

Steroid-Induced Myopathy.—Although the administration of corticosteroids and their derivatives can be lifesaving, unusual but fortunately rare side-effects continue to be reported. Triamcinolone, which has now been on trial for nearly two years, appears to have side-effects not previously noted with other steroids. In addition to the postprandial flushing, headache, loss of weight, and muscular weakness noted by earlier workers, Williams described three cases of myopathy occurring after administration of this steroid (*Lancet* 1:698, 1959). Within three weeks of commencing treatment with this drug the patients complained of muscular weakness, which fortunately disappeared in two of them when the drug was replaced by prednisolone. In the third, assessment of change in the myopathy was difficult because the patient's condition deteriorated. Electromyography showed evidence of a primary muscle fiber lesion, with additional features indicating the so-called neuromyopathic lesion characteristic of polymyositis. Muscle biopsy specimens in two of the patients showed widespread muscle damage, similar to that induced in animals by massive doses of cortisone. Admittedly the dose was larger than that usually used.

Although the muscles of the shoulder girdle were affected, the weakness was greatest in those of the trunk and pelvic girdle. This proximal muscle syndrome closely resembled that seen in the muscular dystrophies and in those myopathies, presumed to be of metabolic origin, which sometimes complicate thyrotoxicosis and malignant disease. Steroid-induced myopathy of this extent must be rare, but it should be considered in a patient given this steroid who complains of muscular weakness and in whom the serum sodium and potassium levels are normal. MacLean and Schurr (*Lancet* 1:701, 1959) described a patient who developed muscular paralysis after taking fludrocortisone for a year. There was a dramatic improvement within three days of stopping the drug.

Aspirin and Gastric Hemorrhage.—Of a group of 106 patients hospitalized for gastroduodenal hemorrhage 54% were found by Muir and Cossar (*Lancet* 1:539, 1959) to have taken aspirin within 48 hours of their first hemorrhage, compared with 15% of a control series hospitalized for miscellaneous conditions. These figures strongly support the contention that aspirin is a potent factor in this type of bleeding. The group of patients who most commonly gave a history of taking aspirin before the hemorrhage were those with acute gastric lesions. About half of those who suffered from bleeding after taking aspirin admitted that it gave them indigestion, and when taken on an empty stomach it was often followed by gastroduodenal hemorrhage. Crushing the tablets made little difference in the irritant action. The authors concluded that aspirin was a dangerous drug, particularly for those in whom it caused gastric pain and in those with a known peptic ulcer. In their opinion about one gastroduodenal hemorrhage in eight is precipitated by aspirin.

Aspirin as Substitute for Insulin.—It has been shown that aspirin can control hyperglycemia and glycosuria and abolish moderately severe ketosis in diabetes. The disadvantages of the treatment of diabetes with aspirin include the early development of nausea, vomiting, tinnitus, and deafness. These symptoms need not arise if the dosage of aspirin is controlled by serum salicylate estimations. The practical value of aspirin in diabetes, however, cannot be decided until its effectiveness has been compared with that of insulin. Reid investigated the insulin equivalence of aspirin in 14 diabetic patients needing from 14 to 112 units a day (*Brit. M. J.* 1:897, 1959). The amount of insulin that could be replaced by a maximum tolerated course of aspirin was determined for each patient. Their ages ranged from 33 to 74 years, the duration of the disease from 1 to 24 years, the carbohydrate intake from 104 to 295 Gm. daily, and the total calories from 1,300 to 2,700 daily. It was thought that the group represented a fair cross section of diabetic patients requiring insulin. After a control period of at least 10 days aspirin was given until a serum salicylate level of 35 to 45 mg. per 100 ml. was attained, and insulin was slowly withdrawn if warranted by the biochemical findings. The amount of insulin that could be replaced by maximum therapeutic doses of aspirin was thus determined for each patient.

Of the 14 diabetic patients 9 who were well controlled with insulin also had good responses to aspirin. The largest quantity of insulin zinc suspension that could be completely replaced by aspirin was 48 units, and the largest reduction in insulin requirement was 72 units, in the patient receiving the largest dose (112 units daily). Five patients who were poorly controlled with insulin were not materially improved by treatment with aspirin. Reid concluded that aspirin was most effective in patients who responded well to insulin and vice versa. The findings in patients well stabilized with insulin also suggested that the greater the insulin requirement the greater the amount of hormone that may be replaced by aspirin. These results place aspirin and salicylates in the class of promising orally administered antidiabetic substances, and should stimulate investigators to find out how they act and to remove undesirable effects.

Medicine in Russia.—Dr. J. B. Harman described his impressions of medical practice in Moscow and Leningrad (*Lancet* 1:725, 1959). Most of the doctors he met were anxious to talk about the work they were doing. Inquiries were made to see if postgraduate medical students from the West could spend a few months working in Russian hospitals and research institutions. This idea was not encouraged. Dr. Harman found Russian practice to be fairly sound as judged by Western standards. A few useless therapeutic relics were still employed, such as dry cupping to prevent pneumonia, inhalations of garlic for the treatment of bronchiectasis and the intravenous administration of bromide, and spa treatment was held in high regard.

One advantage of Russian medicine, from the viewpoint of scientific study if not the patient's welfare, was the opportunity of collecting special cases from the whole of the Soviet Union. Patients are transported in much the same way as political prisoners. In one hospital the author found 200 patients with pituitary basophilism. Laboratories for routine tests were small and decentralized. Apparatus for electrocardiography, electroencephalography, and diagnostic procedures were old-fashioned, and radiotherapy as practiced in the West was limited.

The author's general impression was of medicine from textbooks, rather than from up-to-date journals. The introduction of antibiotics, corticosteroids, and radioactive isotopes has been delayed in Russia, in spite of the availability of Western medical literature. All important articles are translated, abstracted, and distributed to those interested. The author was struck by the fact that Russian medical care was the same as standard orthodox Western medical care. In medicine the Russians appear to techniques, or drugs of their own. The practice be mere copyists and have no new discoveries, of medicine was the same as in an ordinary hospital in Great Britain. In the clinical field the author did not meet a single new idea—good, bad, provocative, ingenious, or even ridiculous. Except in psychiatry everything was all quite orthodox, with no hint of research, criticism, or enthusiasm. No attempts were made by the Russian doctors to obtain any information about Western medicine.

Psychiatry and psychosomatic medicine were exceptions to these generalizations. Freudian psychology is anathema. The work of Pavlov has been applied to experimental and psychosomatic medicine. The conditioned dog is still the basis of experimental psychology. In psychiatry insulin treatment is used extensively, electroshock therapy sparingly, and lobotomy not at all. In a centrally controlled state the direction of research efforts is determined almost entirely by a system of priorities and up to now internal medicine has had a low priority; hence the copying of Western medicine. The author expressed doubt that medicine in Russia is attracting recruits of the right caliber. At the moment it is certainly no place for a medical pilgrimage.

MISCELLANY

A JUNIOR SCIENCE PROGRAM

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In June, 1957, two junior high school students began a summer of study at the research laboratories of the National Children's Cardiac Hospital to learn about research at first hand. Their work provided great promise for using this type of approach in the early training of specially gifted students who are interested or may be motivated to develop interest in science.

Many individuals and agencies were apprised of the program. The declared purposes were (1) to develop laboratory skills, (2) to develop new understandings about the research projects under way in the laboratory, and (3) to permit students to participate in special demonstrations of scientific research in progress.

The hope was to inculcate young, ambitious, capable students with the need for, value of, and interest in adequate scientific education; to serve as a medium for attempting to make available science scholarships for students who otherwise might be unable to obtain a college education in science; to provide science education early in life so that the student, on arriving at age 25 or 26, would be more advanced than the average student of the same age today; and to furnish the opportunity for these science students to maintain a normal social life, by including their science program in the regular school day and allowing normal social after-school activities.

Method

Students in the junior and senior classes of high school were eligible for participation. The school science supervisors made recommendations to the school principals. If they approved, the applications were transmitted to the Dade County Board of Public Instruction where they came to the attention of the curriculum director and the county science supervisor, in accordance with instructions from the assistant superintendent for general education. All prospective students were interviewed jointly by the county school science supervisor and the director of the junior science program.

Individual requirements included good health (excellent school attendance record, no serious physical disabilities, sound eyesight, good neuromuscular coordination), favorable character traits (high persistence, attitude toward failure as a challenge rather than as a disappointment, physical and mental drive, intense interest in science, ability to cope with responsibilities), achievement (IQ of at least 135 on the California test[1] or 120 on the Otis Beta,[2] acceleration of at least two grade levels in mathematics and three grade levels in verbal ability, and completion of at least one year of laboratory science and one year of high-school mathematics), parental consent, time available from the regular school day (one or two class periods), and transportation.

Each applicant was asked his particular interest in science. The school and program authorities reviewed the requests and curriculums of the students. The program director then contacted various research laboratories in Miami, trying to place each participant in an institution convenient for transportation and in which the desired type of project could be followed.

Originally, the students were to spend four afternoons a week in the laboratory and the fifth in observing a demonstration. This proved too much of a burden on both scientist and novice, so that the second year of operation found the students spending at least two of the afternoons in the laboratory and the remaining sessions in the library reading and studying material, on an unassigned basis, pertinent to their projects.

Director of Medical Research, National Children's Cardiac Hospital.

During the first year (1957-1958) most of the time was spent didactically, while in the second year (1958-1959) the students were treated as mature researchers and were given every assistance they sought. They quickly developed their own programs, however, and worked with a minimum of supervision.

Laboratory facilities thus far utilized include microbiology, enzyme chemistry, meteorology, virology, cardiac surgery, and cancer research. As the junior science program expands there is almost no limit to the biological science facilities available. Because of our interest in biological sciences we made few attempts to establish physical science laboratory contacts.

Results

Eight students from three high schools were the first group to participate. Two boys failed to complete the period; their selection was not based on the rigid criteria later established, as set forth above. One girl, originally undecided as to whether she desired a career in science or in home economics, came to the conclusion she preferred the latter. Four additional participants, two boys and two girls, are preparing for the study of medicine. One girl, both of whose parents are social workers, plans to continue her studies in basic biological science.

The current year involved 34 applicants, but proper placement was arranged for 12. One student refused her assignment, and another dropped out shortly after the beginning of the school year. Two boys are carrying on a research project at a United States Weather Bureau station. One girl is working in the surgical cancer research laboratory of the University of Miami Medical School; one boy is in the cardiac surgical laboratory of the medical school. His project is the determination of the optimal blood flow in a new type of pump oxygenator for maximal oxygenation. The remaining six students are working in the research bacteriology laboratory of the National Children's Cardiac Hospital. One student is studying the effect of electricity on the growth of bacteria; another is attempting to produce a strain of beta hemolytic streptococci reacting to groups A and F antiserums simultaneously; a third is attempting to develop bacteriological techniques which will make the determination of the rate of recovery of beta hemolytic streptococci more accurate; a fourth is assaying various components of synthetic mediums to determine the minimum growth requirements for beta hemolytic streptococci; a fifth student, using synthetic mediums, is studying the effects of altering the ratio of glucosamines to glucose on the group specificity of beta hemolytic streptococci; and the sixth is observing the utilization and transfer of glucose by beta hemolytic streptococci by means of radioisotopic techniques.

Comment

Many of our educational systems are based on providing facilities for the average student, and additional help is available generally for retarded students, yet very few areas spend much effort on the gifted student. The young excellent or superior scholar frequently wastes much of his day in the classroom, either in inattention or in troublemaking. Sometimes a gifted person is advanced beyond his regular class and, in such a case, his social adjustment may suffer.

School systems throughout the United States are beginning to realize the shortcomings of preparation for scientific careers for gifted students. The Bronx High School of Science is one kind of answer to this problem. Individual schools have adopted a variety of approaches to better scientific education. In Miami, students may spend a portion of the regular school day profitably in learning research techniques in operating research laboratories. Description of the project has been published by West[3] in journals devoted to education. A report also appeared in a publication of the National Science Teachers Association.[4]

The program has provided such stimulation to the students that 5 of this year's participants entered the Westinghouse Talent Search competition, and all 10 are expected to enter the annual science fair. All but one are planning careers in the biological sciences.

No major effort has been made to include the physical sciences in the Junior Science Program, although obviously this should be done. The preparations for adequate activities, arrangements with suitable laboratories, and supervision of the students require a full-time competent instructor. This need has not been met to date, and has somewhat curtailed the project. Efforts are now being made to correct this defect. Eventually, course credit may be offered toward high school graduation.

Summary

A program has been developed in Dade County, Florida, in close cooperation with the board of public instruction, to teach gifted high school students not only scientific research methodology but also scientific thinking. This instruction is through on-the-job observation and performance with supervised execution of individual research projects, and it is integrated into the regular school day's schedule.

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MEDICAL LITERATURE ABSTRACTS

INTERNAL MEDICINE

Left Atrial Thrombosis: Its Preoperative Diagnosis. A. Jouve and P. Rochu. Semaine hôp. Paris 35: 406-409 (Feb. 4) 1959 (In French) [Paris].

The authors studied the statistical probability of preoperative diagnosis of left atrial thrombosis by reviewing its incidence in 200 patients who were operated on for mitral commissurotomy. Age of over 35 years, permanent atrial fibrillation, absence of mitral valve insufficiency accompanying mitral stenosis, and embolic disorder of the systemic circulation were identified as factors contributing affirmatively to the preoperative diagnosis of left atrial thrombosis. A radioscopic record in which the left atrium was found bulging and without visible pulsation, combined with absence of visualization of the left atrium by angiocardiography, had a high indicative, but not conclusive, value for the preoperative diagnosis. Change in the auscultatory pattern, presence of paroxysmal mitral occlusion as described by Mahaim, and roentgenologic signs of calcification in the left atrium were rare and unreliable diagnostic indicators. This investigation reveals that in most instances it is probable, but not certain, that a diagnosis of left atrial thrombosis will be made before operation in patients with mitral stenosis.

Magnesium Depletion in Man. R. E. Randall Jr., E. C. Rossmeisl and K. H. Bleifer. Ann. Int. Med. 50:257-287 (Feb.) 1959 [Lancaster, Pa.].

The symptoms of psychiatric and neuromuscular disorders reported to be associated with low serum magnesium concentrations have included delirium, confusion, muscle tremors, cramps and twitchings, choreiform and athetoid movements, and, rarely, convulsions. While these symptoms have, in general, disappeared after magnesium therapy, insufficient data have been presented to document conclusively a state of magnesium depletion causally related to the observed symptomatology. The present report includes observations on 12 patients with similar neuromuscular and psychiatric abnormalities and associated disturbances in magnesium metabolism. In 10 instances the serum magnesium concentrations were notably depressed. Balance data gave evidence for depletion of the total body magnesium in several patients, and a disordered metabolism of calcium was apparent in all. The data on 3 patients are presented in detail, and the pertinent features of all cases are reviewed.

Clinical improvement, which was sometimes dramatic, was observed after the administration of magnesium by the parenteral route or in the diet. Abnormal electroencephalograms and electrocardiograms improved after therapy in several instances. Calcium administration alone failed to correct the neuromuscular disorder in 2 of these patients, and it may actually have intensified the symptoms. Magnesium administration usually resulted in a positive magnesium balance, on occasion associated with significant increases in the serum calcium concentration and in the renal excretion of calcium. Clinical features, probably concerned in the etiology of the presumed magnesium depletion, were severe malnutrition and usually some loss of fluid and electrolytes, such as vomiting or diarrhea. Excessive renal excretion of magnesium, observed in one patient, is thought to have been related to potassium depletion. While it is not clear how magnesium depletion produces symptoms, evidence suggests that an intracellular depletion of this ion is of primary significance. Increased awareness of the clinical importance of magnesium and improved techniques for studying the distribution and function of this ion will undoubtedly clarify the precise role of the magnesium ion in disease states. At the present time, however, it is clinically important to recognize the possibility of magnesium deficiency as a causative factor in disturbances of neuromuscular and central nervous system activity, particularly in patients with malnutrition.

Tuberculous Meningitis in Adults: Anatomic, Pathological and Clinical Findings. G. Galzerano and R. Sorrentini. Arch. tisiol. 13:1039-1050 (Nov.) 1958 (In Italian) [Naples].

Autopsy records of 93 hospitalized patients who died of tuberculous meningitis during the past 17 years were reviewed to analyze the anatomicopathological lesions of the disease. This number of deaths represents only 2.14% of all deaths attributed to tuberculosis. The death rate was highest among

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the youngest patients and decreased in the older age groups. Tuberculous meningitis was related to the primary phase of the disease in 2 patients and to the postprimary phase in 90; it was unrelated to any other tuberculous process in 1. The incidence of tuberculous meningitis was connected with an early tuberculous infiltration in 3 patients, a tuberculous nodular process in 30, a miliary process in 29, pleursy in 19, and an extrapulmonary process in 9.

The tuberculous process in the meninges developed simultaneously with that in another part of the body in 84 instances, and it developed subsequently to it in 8. The tuberculous process took place mostly in the leptomeninges at the base of the brain, less frequently in the meninges of the vault of the cranium, and rarely in the meninges of the spinal cord. The frequency of the lesions in the meninges of the vault has increased per number of patients, whereas that in the meninges at the base has remained almost unchanged since the advent of antibiotics, as compared with the previous period. Change of the exudate from fibrous organizations to such formations as predispose to development of various hydrocephalic syndromes was the most significant change in the anatomicopathological picture of tuberculous meningitis since the advent of antibiotics. Involvement of the ependyma in the process of the tuberculous meningitis, which developed in 8 patients during the antibiotic era, had not been previously observed in this series of patients.

Hyperaldosteronism with Adenomatous Hyperplasia of the Adrenals in a Hypertensive Patient with Refractory Edema. R. S. Mach, A. Fanconi, A. F. Muller and others. Schweiz. med. Wchnschr. 89: 98-102 (Jan. 24) 1959 (In French) [Basel, Switzerland].

The authors review the various clinical conditions of patients with hyperaldosteronism. They suggest classification of these cases into 4 groups: (1) hyperaldosteronism caused by an adrenal cortical tumor, associated with arterial hypertension, polyuria, transitory paralysis, potassium depletion with hypokalemia, and intracellular sodium retention without edema (Conn's syndrome); (2) hyperaldosteronism caused by an adrenal cortical tumor, associated with sodium and water retention in the interstitial spaces but without hypokalemia; (3) hyperaldosteronism without adrenal cortical tumor, but associated with edema of unknown origin (called idiopathic edema by dysfunction); and (4) secondary hyperaldosteronism as a consequence of edema of known origin, often associated with a cardiac or a renal or a hepatic disease.

A detailed description is given of a 55-year-old man who had arterial hypertension of 10 years' duration, with the consequent development of left cardiac insufficiency and rapid extension of edema refractory to all treatment. The patient had an enlargement of the liver and, in addition, suffered from orthopnea, insomnia, and nausea. Laboratory values revealed hyperaldosteronuria, ranging from 40 to 96 mg. in 24 hours, and a very low urinary excretion of sodium, sometimes between 1 and 4 mEq. in 24 hours. The plasma electrolytes including bicarbonates were normal except after the administration of mercurial diuretics when a mild hypokalemia and hypochloremia appeared. The urinary output of potassium was in proportion to the patient's food ingestion, and showed values ranging around 50 mEq. in 24 hours. Autopsy revealed adenomatosis of both adrenals with multiple tumors the size of a hazel-nut, cardiac hypertrophy with fibrosis in the region of the large vessels, and diffuse arteriosclerosis with arteriosclerosis of the kidneys. The role of hyperaldosteronism and that of cardiac insufficiency in the pathogenesis of edema are discussed.

Clinical and Morphologic Aspects of Macroglobulinemia of Waldenström: Concerning 10 Unpublished Observations. L. R. Wasserman, G. Gelin, S. Lee and others. Sang 29:633-665 (no. 8) 1958 (In French) [Paris].

This report presents the clinical, cytological, and anatomic studies made on 10 patients with macroglobulinemia of Waldenström. The disease is a particular lymphoreticulosis, indicating a relationship, on the one hand, with multiple myeloma and, on the other, with chronic lymphoid leukemia and possibly with other malignant tumors. On the clinical plan the disease is characterized by its predilection for persons of the older age group, by frequent hemorrhages, by the decrease in the number of erythrocytes and sometimes of leukocytes and blood platelets, and by a tremendous increase in the sedimentation rate. Serum electrophoresis reveals an abnormal peak in the beta or gamma globulins. Ultracentrifugation usually discloses globulins of high molecular weight around one million. The bone marrow shows infiltrations of lymphocytes or reticular lymphocytes and the presence of tissue mast cells.

From the standpoint of anatomy the most characteristic feature is undoubtedly represented by the dissemination of a particular lymphoid or reticular lymphoid tissue in the whole organism but especially in the bone marrow, the lymph nodes, the spleen, the liver, and the kidneys. Further studies are necessary to recognize the histogenesis and significance of this proliferant tissue. Macroglobulinemia may be classified into 2 types; the malignant form, leading in less than 2 years to death, and the relatively benign form, with a gradual development, lasting for 6, 10, and even 15 years. There is no specific treatment for this disease; transfusions are indicated after hemorrhages and may be beneficial in patients with the latent form of the disease. Steroid therapy is useful only in patients with macroglobulinemia associated with considerable hemolysis. Splenectomy is indicated only in patients with a greatly enlarged spleen or in those with imminent thrombocytopenia.

Type D Hemoglobin in an Italian Family of Calabrian Origin. E. Silvestroni, I. Bianco and M. Muzzolini. Policlinico (sez. prat.) 66:41-50 (Jan. 12) 1959 (In Italian) [Rome].

In a statistical study on hemoglobin abnormalities made among the population of southern Italy and of insular Italy, one subject, out of 2,186 persons examined, was found to be a heterozygote carrier of an abnormal hemoglobin which because of its characteristics could be classified as type D hemoglobin. A study was then carried out among the relatives of this subject, a 44-year-old man, and among them 5 additional heterozygote carriers of type D hemoglobin were found. Three belonged to the family of the subject studied (the father, a brother, and a nephew), and 2 to the family of one of his uncles (the uncle and a cousin). The 5 relatives showed no signs of blood disease; all blood findings were normal. In each of these subjects it was found that the type D fraction represented 37 to 45% of the entire hemoglobin. The intracorpuscular crystallization of hemoglobin was easily demonstrable in all subjects. The spectrophotometric study in ultraviolet of the type D fraction isolated by electrophoresis on starch and the study of its behavior in the presence of alkalies showed no significant differences as compared with type A hemoglobin. The genetic study of the entire family strain confirmed the hypothesis that in hereditary transmission type D hemoglobin behaves as a Mendelian dominant character.

Myocardial Infarction: A Clinical Study of 153 Cases in the Philippine General Hospital. E. Z. Fang, J. M. Barcelona, J. R. Bobadilla and others. Acta med. philippina 14:71-111 (Oct.-Dec.) 1957 [Manila].

The objectives of the studies reported here were, first of all, to confirm or disprove some widely held impressions concerning myocardial infarction. These were that the incidence (1) varies considerably in different parts of the world, (2) has increased in recent years because of some changing factors in our civilization, such as the consumption of fats, dairy products, or tobacco, (3) is much higher among men than among women, (4) reaches a peak at a later age in women than in men, (5) is higher in the upper socioeconomic groups than in the lower, and (6) is higher among persons with diabetes mellitus than among persons without diabetes. The authors also wanted to compare the figures obtained in the Philippines with those obtained by the American Heart Association and American authors. Finally, they hoped to find common denominators among the fatal cases which might serve as prognostic criteria.

The material on which this study was based was obtained from the Philippine General Hospital in Manila. Studies on 153 patients with myocardial infarction revealed that the average age was 59.7 years, that of male patients being 58.8 years and that of female patients, 63.5 years. These figures tally closely with those reported by American authors. The ratio of male to female patients was about 4:1. The authors feel that they are not in a position to confirm or disprove the statement of higher incidence of myocardial infarction among those in the higher socioeconomic strata. They found the incidence to be fairly significant in the lower economic strata, especially among those who were undernourished and overdrained in their physical resources.

About 70% of the patients had a previous history of coronary artery disease, and the incidence increased with age from 33.3% in the 4th decade to 100% in the 9th decade. About 42% of the patients had a history of hypertension; it reached a peak of 52% in patients in the 6th decade and declined at higher ages. The ratio of incidence of preexisting hypertension between female and male patients was about 2:1. All these figures tally closely with those reported by American authors. A history of diabetes was obtained in 9% of the patients; this figure is low when compared with the figures of American authors. The fatality rate was higher among those with than among those without diabetes. The authors observed a higher incidence of anterior infarction than did American investigators.

No provocative factor could be ascertained in the majority of the acute cases; in 4% the onset was painless; all had severe dyspnea. The authors agree with American investigators that, while pain is less intensively felt among the aged, dyspnea is more frequently experienced. Pain and dyspnea were more severe in the fatal cases. The death rate was high among the patients admitted with a temperature of 36.5 C (97.7 F) or lower. There was no significant difference in fatality between those with a normal pulse rate and those with a pulse rate over 100. There were no deaths among those admitted with bradycardia.

Drop of the systolic blood pressure in acute myocardial infarction indicated a poor prognosis. There was a slightly higher incidence of cardiac enlargement among the female than among the male patients, probably attributable to the higher incidence of hypertension in the former. Two-thirds of the fatal cases had cardiac enlargement. The degree of leukocytosis and its duration were related to the size and location of the infarcted area. Leukocytosis indicated a poor prognosis, in that 77% of the patients who died had that condition. Azotemia also was frequent in the fatal cases. Death usually followed within 24 hours after the acute onset. In those who survived, the acute symptoms were usually under control within 3 days.

Diet and Diabetes. E. Azerad and Goarant. Presse méd. 67:243-244 (Feb. 7) 1959 (In French) [Paris].

The necessity of a special diet in patients with diabetes is generally accepted; its importance, however, has been overestimated. Glycemia and glycosuria levels do not always vary in proportion to the ingested amount of carbohydrates. The authors investigated the influence of breakfast in patients with diabetes and noted that this small food ingestion, although it consisted according to French traditions of only a restricted quantity of carbohydrates (25 to 35 Gm.), precipitated significant and more elevated hyperglycemic levels than those observed after the consumption of a lunch composed of higher glucide values. Urinalysis for sugar, performed every 15 minutes in these patients treated with diet alone, showed increased glycosuria levels between 1 and 2 hours after breakfast. The glycemic curve showed a maximum peak around an hour and a half after breakfast and returned to the initial fasting values, sometimes even below normal levels, 4 hours after breakfast. Studies of the effect of other meals will be reported later. The findings already obtained make it clear that the largely accepted notions concerning diet for diabetic patients should be revised, and that the effect of meals on glycemia and glycosuria should be systematically investigated, so that a few practical rules can be formulated.

The Diagnostic and Therapeutic Value of Thyrotropic Hormone and Heavy-Dosage Scintigrams for the Demonstration of Thyroid Cancer Metastases. B. Catz, D. Petit and P. Starr. Am. J. M. Sc. 237: 158-164 (Feb.) 1959 [Philadelphia].

The cases of 6 women and 2 men, between the ages of 23 and 75 years, are reported as illustrative of those of 44 patients with thyroid cancer who were treated at the Los Angeles County Hospital. After surgical removal of all resectable thyroid tissue, cancerous and normal, the patients received 10 units of thyrotropin intramuscularly for 5 to 7 days, after which 1 to 2 mc. (tracer dose) of radioiodine (I^{131}) was given by mouth. Total body scanning and routine scintigrams of the neck, chest, and metastatic sites were then done. If there was any evidence of the collection of I^{131} by residual tissue in the neck or metastatic sites, a therapeutic dose of I^{131} (40 to 100 mc.) was given. Seven days later a repeat scanning was taken and a scintigram was made to establish the precise collection of the isotope with the larger dose. Twenty-four-hour uptake of I^{131} and 72-hour excretion studies were done with a dose of 100 mc. of I^{131}.

The decision to treat patients with thyroid cancer with I^{131} is based on the demonstration of thyroid tissue and proof of its avidity for I^{131}. The scintigrams made in these patients after administration of 50 to 70 units of thyrotropin, causing proper stimulation of scanty residual tissue, showed "functioning" thyroid tissue, when conventional uptake and excretion studies gave negative results. The diagnostic value of large-dose scintigrams has been established, since without this procedure many patients would not have been treated in the presence of thyroid tissue. These studies also revealed that there was a lack of correlation between the histological diagnosis of the original cancer and the collection of I^{131} by the metastatic tissue. Evidence is at hand in other studies that 66% of the patients in whom metastases have been found by the technique of heavy doses of I^{131} and thyrotropin have subsequently had negative scintigrams. The assumption has been made that this represents total ablation of the tissue.

Conservative Treatment of Pancreatitis: Statistical Information. F. R. Mathiesen. Ugesk. laeger 121: 161-165 (Jan. 29) 1959 (In Danish) [Copenhagen].

From 1937 to 1956, 171 patients with acute pancreatitis were treated in the Copenhagen Municipal Hospital. The treatment was predominantly conservative. There were 10 deaths. Seven patients were operated on in the acute stage, with 2 deaths. The low frequency of operation is believed to have played an essential part in the low mortality. Diastase values over 1200 to some extent weaken the prognosis, and a palpable resistance in the epigastrium aggravates it further. There was resistance in 6 of the fatal cases but in only 21 cases in the entire material. The clinical course in the 10 patients who died points to the central significance of shock, but successful treatment of the shock does not insure against fatal outcome.

Pulmonary Infections Complicating Asian Influenza. R. G. Petersdorf, J. J. Fusco, D. H. Harter and W. S. Albrink. A. M. A. Arch. Int. Med. 103:262-272 (Feb.) 1959 [Chicago].

During the Asian influenza epidemic in October, 1957, 91 patients with pulmonary infection associated with influenza were admitted to the Grace-New Haven Community Hospital, New Haven, Conn. Of these, 38 had bacterial pneumonias, 24 of which were due to Diplococcus pneumoniae, 6 to Staphylococcus pyogenes var. aureus, and 6 to Hemophilus influenzae. In 43 patients with pulmonary infiltrates, no specific pathogenic bacteria seemed to be present. Ten patients manifested only severe tracheobronchitis. It was not practicable to attempt to demonstrate influenza virus infection in every one of the 91 patients. Blood for hemagglutination inhibition tests and throat washings for virus cultures were obtained in a number of instances to show that such an infection had been present. These findings, when added to the epidemiologic data, make it appear almost certain that the Asian influenza virus was a factor in the pathogenesis of the majority of these infections. In about one-half of the cases symptoms of typical influenza preceded the appearance of pneumonia, while in the remainder the illness began with symptoms attributable to pulmonary infection. Cough and fever were present in almost all the patients, while pleuritic pain and rigors were seen primarily in those with bacterial pneumonia. Bloody sputum was present in 5 fatal cases and was an ominous prognostic sign, as was leukopenia. Pregnant women and patients with heart and chronic pulmonary disease seemed to be unusually susceptible to postinfluenza pneumonia.

Antimicrobial therapy in 28 of 38 patients with bacterial pneumonia resulted in defervescence within 72 hours. Twenty-four of 43 patients with pneumonia of undetermined etiology also improved rapidly on antibiotics. A number in this group, however, did well in the absence of chemotherapy. Eleven patients died; 4 were older persons with serious chronic disease, but 7 were previously healthy adults who had a fulminating illness characterized by severe toxicity, bloody sputum, high fever, leukopenia, anoxia, and circulatory failure. Antibiotics, adrenocortical hormones, and other supportive measures were ineffective. Autopsy on these patients revealed a hemorrhagic necrotizing pneumonia, and staphylococci and influenza virus were isolated from the lungs of 3 patients. The uniformity of the clinical and pathological picture in this group suggests that the virus is the primary etiological agent in pneumonia associated with influenza.

Hepatolenticular Degeneration (Wilson's Disease): A Case Diagnosed Biochemically before Clinical Manifestations. T. Lygren, E. W. Sörensen and A. Bernhardsen. Lancet 1:276-277 (Feb. 7) 1959 [London].

With the use of Ravin's colorimetric technique as a screening test, the authors studied a patient who had a low serum copper oxidase activity but no symptoms or signs of hepatolenticular degeneration. When first examined in August, 1956, the patient was 23 years old. He had had infectious hepatitis at the age of 3 years but no liver disease or any other serious illness since then; there was, however, a family history of hepatolenticular degeneration. Fourteen months later his liver and spleen were palpable, but he was still feeling well; potassium sulfide and a high-protein diet were prescribed. The patient continued to work as a fisherman until January, 1958, when he began to suffer from diffuse abdominal pain and distention. When he was hospitalized in February, 1958, he had no neurological or mental symptoms, and slit-lamp examination failed to disclose a Kayser-Fleischer ring. Yet he had edema and gross ascites and was jaundiced; he became stuporous and died 15 days later. Autopsy revealed nodular hepatic cirrhosis and enlargement of the spleen. The diagnosis was portal cirrhosis due to hepatolenticular degeneration (Wilson's disease).

Ravin's colorimetric method of serum copper oxidase estimation is a good screening test, not only when symptoms or signs are already present but also when investigating symptomless members of affected families. Despite impaired liver function, abnormal aminoaciduria was absent in this patient 3 months before he died; it developed while he was under observation; and it diminished for glutamine, serine, taurine, and methylhistidine in the terminal stages of his illness. The pattern of aminoaciduria seems to vary: the patient presented excreted an unusual amount of alpha-amino-*n*-butyric acid. The authors can suggest no explanation for this; nor do they know why aminoaciduria developed so late.

Chronic Renal Disease with Secondary Hyperparathyroidism. V. E. Pollak, A. F. Schneider, G. Freund and R. M. Kark. A. M. A. Arch. Int. Med. 103:200-218 (Feb.) 1959 [Chicago].

Since abnormalities of the skeletal system, including osteitis fibrosa, are known to occur in patients with chronic renal disease, and since osteitis fibrosa occurs only in connection with primary or secondary hyperparathyroidism, the authors consider it surprising that the literature reports so few instances of renal disease with secondary hyperparathyroidism. Although only 25 well-documented examples of hyperparathyroidism secondary to renal disease were found in the literature, the authors found evidence of secondary hyperparathyroidism in 17 of 91 consecutive patients dying of chronic renal disease. All patients discussed in this paper had postmortem evidence of (1) chronic renal disease, (2) significant enlargement of 2 or more parathyroid glands, and (3) osteitis fibrosa. Severe bone lesions were observed in 5 of the 17 patients, and lesions of mild to moderate severity in 12 instances. The commonest renal lesion was pyelonephritis, either alone or in combination with other lesions. Congenital lesions were also frequently observed. The incidence of uncomplicated glomerulonephritis was comparatively low. Secondary hyperparathyroidism occurred particularly in the second and third decades of life and frequently in patients with renal disease of long duration. The serum calcium level was often normal or elevated and was significantly higher than in a comparable group of patients with renal failure who did not have secondary hyperparathyroidism. Ectopic calcification occurred in most patients.

The history of one of the patients, an 18-year-old woman, is reported in detail. She entered the hospital with severe azotemia, anemia, and widespread osteitis fibrosa cystica. The differential diagnosis between primary renal disease with secondary hyperparathyroidism and parathyroid adenoma with secondary renal disease presented some difficulty; severe chronic pyelonephritis was diagnosed by renal biopsy. The patient died of uremia 11 months later, by which time the osteitis fibrosa had progressed even further. At autopsy it was found that all 4 parathyroid glands were greatly enlarged; the diagnosis of osteitis fibrosa cystica was confirmed, and small congenital polycystic kidneys, with severe, acute, and chronic pyelonephritis, were found.

SURGERY

Results of Treatment of Aneurysm of the Abdominal Aorta. D. P. Boyd and H. Pastel. Postgrad. Med. 25:238-242 (March) 1959 [Minneapolis].

Twenty patients (16 men and 4 women), between the ages of 45 and 79 years, with aneurysm of the abdominal aorta, underwent resection of the aneurysms with insertion of homografts. The aneurysms in 19 patients were caused by arteriosclerotic disease. Symptoms attributable to the aneurysm consisted of abdominal pain in 13 patients and abdominal pulsation in 4; only 3 patients did not have any preoperative symptoms. The most difficult part of the operation was separating the inferior vena cava from the aneurysm. Surgical intervention was associated with complications in 14 patients, and 8 of these had either arterial or venous thrombosis. Two patients died in the immediate postoperative period, one of hypertensive cerebral disease and the other of anuria, pancreatitis, and gangrene of the left leg. Seventeen of the 18 patients who survived were followed for more than one year. There were 3 late deaths: One patient died of myocardial infarction 8 months after the operation; the second patient died of a hemorrhage into the distal portion of the duodenum from the site of the upper anastomosis 2½ months after the operation; and the third patient died of myocardial infarction which occurred 3 weeks after a second operation for a hemorrhage similar to that in the preceding patient.

The results were excellent in 13 of the 15 patients who were known to be living when this paper was written and who were free of symptoms. The results were unsatisfactory in 2 patients, with mild claudication on exertion in one and with amputation because of a thrombotic complication in the other. Although the interval since resection of the aneurysms and insertion of homografts has not been long enough in this series to warrant definite conclusions regarding the value of the operation, the results, as judged by the period of survival and the relief of symptoms, appear to justify the use of this operative procedure. The authors believe that asymptomatic aneurysm should be resected if the condition of the patient will permit this operation.

Assessment of Varicose Veins with the "Retrograde Leg-milking" Test. J. A. Gius. Postgrad. Med. 25: 267-273 (March) 1959 [Minneapolis].

Modern therapy of varicose veins involves ligation and stripping of all abnormally dilated veins, and its success depends on the completeness with which the sites of valvular incompetency are interrupted. The pattern of valvular insufficiency and varicose veins varies greatly from patient to patient, and detailed studies of the venous circulation should be carried out with respect to sites of valvular insufficiency before operation.

To identify and localize valvular incompetency, the author recommends the "retrograde leg-milking" test, which is performed with the patient standing on a low platform or chair and with the lower extremities exposed to the groin. The examiner, who is seated facing the patient, first observes and palpates both saphenous systems and all varicosities, and notes any skin changes in the legs. A segment of rubber tubing is then applied around the leg, just above the lowest cluster of varicosities, tightly enough to occlude the superficial but not the deep veins. The tourniquet should be fixed with a hemostat to prevent slippage. The milking maneuver is performed by the examiner, who encircles and compresses the tissues at the patient's ankle and rapidly moves his hands upward to the level of the tourniquet. The maneuver is repeated 2 or 3 times until all blood is milked from the superficial veins into the deep veins through communicating veins. When milking is complete, it will be observed that the superficial veins are collapsed and that the skin is quite pale in comparison with the pink to cyanotic color of the opposite leg. If the varicosity fills slowly (in about 30 seconds) from below, the implication is that there are no incompetent perforators below the level of the tourniquet. If, instead, there is rapid filling (in less than 10 seconds) confined to the varix, it is probable that an incompetent perforator exists in the region of the varix. Sometimes the presence of a perforator can be further substantiated by palpating a thrill and hearing a decrescendo murmur as the varix rapidly fills with blood. After the area below the tourniquet has been studied, the tourniquet is moved to successively higher levels, depending on the distribution of the varicosities, and the same maneuvers and observations are repeated. Finally, the tourniquet is placed at the upper thigh, the entire leg is milked upward, and the function of the saphenofemoral valve is assessed. If this valve is incompetent, the varicosities will fill by reflux immediately after the tourniquet is released. By this means all possible points of valvular incompetency can be studied under direct vision.

The retrograde leg-milking test actually combines many features of other tests used in the study of varicose veins, such as the Trendelenburg test and the Perthes test. In the leg-milking test, though, the patient does not have to move, but in some cases the Valsalva maneuver may be used to bring out borderline or latent valvular insufficiency. The retrograde leg-milking test is a simple, easily applied maneuver which can be used to identify and localize sites of valvular incompetency.

Studies on Portal Hypertension. A. K. Basu. J. Indian M. A. 32:81-89 (Feb. 1) 1959 [Calcutta].

Thirty-four patients with portal hypertension were operated on in Calcutta, and 26 of these were followed up postoperatively for periods ranging from 6 months to 4 years. Portal hypertension was caused by extrahepatic obstruction in 12 patients, by intrahepatic obstruction in 18, by combined intrahepatic and extrahepatic obstruction in 2, and by suprahepatic obstruction in 2. Splenectomy was performed on 17 patients, splenectomy combined with splenorenal shunt on 11, portacaval shunt on 1, ligation of the hepatic and splenic arteries on 3, and ligation of the splenic artery alone on 1; the operation was not specified for one patient. Of the 26 patients followed up, 21 were doing clinically well; only 3 had recurrent hemorrhages, and ascites developed in 2. Functional as well as structural improvement resulted in some of the patients, in whom cirrhosis of the liver causing intrahepatic obstruction was already observed at operation. In patients with extrahepatic obstruction, the results of operation were even better.

A few significant observations have been summarized. Hemorrhages are commoner with extrahepatic than with intrahepatic obstruction. Ascites seldom occurs with extrahepatic obstruction. The most important diagnostic aid is splenoportal venography, which is simple, is relatively free from risk, and gives significant information with regard to the site and also sometimes the nature of the obstruction. Electrophoretic studies of serum proteins and protein fractions are the best guide to the state of liver function. There is no definite relationship between portal hypertension and the incidence of hemorrhagic manifestations. In the pathogenesis of portal hypertension, the commonest type of obstruction is intrahepatic obstruction due to cirrhosis of the liver. For patients with repeated hemorrhage, splenectomy combined with splenorenal shunt is the operation of choice. Portacaval shunt is indicated for patients in whom the increase in the size of the liver and the increased splenic activity are not significant, or for patients with hemorrhage occurring after splenectomy or splenorenal shunt. Simple splenectomy is indicated for patients without hemorrhage. There is evidence that in many patients reversal of the fibrotic process in the liver occurs after splenectomy and that there is sustained improvement of liver function.

Arterial Bypass Below the Knee. G. C. Morris, Jr., M. E. de Bakey, D. A. Cooley and E. S. Crawford. Surg. Gynec. & Obst. 108:321-332 (March) 1959 [Chicago].

The goal of treatment of segmental occlusive disease of the femoral artery is to restore pulsatile blood flow in the lower leg. In general, use of the bypass principle yields more consistently gratifying results than resection and grafting or thromboendarterectomy. The authors restored pedal pulses in more than 86% of the 317 patients whom they treated by the bypass graft technique for occlusive disease of the femoral artery. The proximal popliteal artery is usually suitable for distal bypass anastomosis, and it can be satisfactorily exposed through a medial thigh incision in conjunction with a femoral incision.

In certain instances the proximal popliteal artery may be unsatisfactory for the distal bypass anastomosis because of arteriosclerotic occlusive disease or aneurysm. Exposure of the distal popliteal artery through a medial thigh incision is difficult, and posterior approach to the popliteal artery is awkward in conjunction with femoral or abdominal incisions. Fortunately, the anatomic arrangement of the upper leg facilitates access to the distal popliteal and posterior tibial arteries through an anteromedial incision below the knee. Such an approach is surgically ideal and anatomically sound; division or splitting of muscles or tendons is not necessary, and there is little or no trauma to the collateral arteries around the knee. The anteromedial incision can be made with the patient supine, in combination with femoral and abdominal incisions. The only satisfactory anatomic path for the bypass tube from the common femoral artery to the infragenual portion of the popliteal artery is through the adductor canal into the popliteal space and behind the popliteus muscle. The bypass tube can be tunneled between these points without difficulty and without an intermediate incision.

Nine instances in which the below-the-knee arterial bypass was used in 8 patients are presented to illustrate the variable application and pathological circumstances in which this operation appeared advantageous. Since these operations were performed, 25 additional patients have been operated on by this method. Late thrombosis occurred in 10 of these 33 patients. Reoperation was performed on 6 patients, with successful thrombectomy and graft replacement in 2. Thus, in 25 of these 33 patients the bypass grafts are still functioning with palpable pedal pulses. Amputation has been necessary in only one instance, and this particular patient had preexisting gangrene of the foot.

Carcinoma of the Pancreas: A Review and Critical Study of 100 Cases. H. D. Gullick. Medicine 38:47-84 (Feb.) 1959 [Baltimore].

This report is concerned with 100 patients treated for carcinoma of the pancreas at the Strong Memorial-Rochester Municipal hospitals, Rochester, N. Y. The diagnosis had been proved by biopsy or autopsy, and the cases had been followed up. Three patients are discussed separately, because they illustrate that there may be unusually long survivals in carcinoma of the pancreas, or that carcinoma may develop in a patient with chronic pancreatitis. The discussion in the main body of the paper is concerned with 97 patients and with literature reports. The natural course of carcinoma of the pancreas with its usually insidious growth and extension was that of rapid hopeless progression, except where modified by radical surgical extirpation in suitable cases. Earlier reporting by the patient and closer scrutiny of clinical details and awareness of the peculiarities of this malignancy by the physician are necessary if the percentage of patients amenable to curative treatment is to be increased.

The duration of symptoms gave no indication of the extent of the disease. Regional lymph node metastases, distant metastases, and invasion of other structures were present as early as 2 weeks after the onset of symptoms. The average time for the appearance of extension of the tumor was 5 months after the onset of symptoms. The predominant pain in carcinoma of the head of the pancreas was in the epigastrium and right upper quadrant; in carcinoma of the body and tail it was in the epigastrium and left upper quadrant. Pain in carcinoma of the head of the pancreas was most frequently aggravated by eating, while pain in carcinoma of the body and tail frequently increased when the patient was in the recumbent position. Extension of the tumor into adjacent organs or numerous metastatic foci occasionally was accompanied by little or no pain. There was a tendency to emotional disturbances of a depressive type in some patients with carcinoma of the body and tail of the pancreas. However, those patients also generally had the cardinal symptoms of abdominal pain and weight loss. In 21.7% of carcinomas of body and tail of the pancreas, but in only 1.6% of those of the head of the pancreas, did symptoms from metastases occur before those of the primary tumor.

It was observed also that jaundice is a primary symptom of carcinoma of the head of the pancreas and may occur while the lesion is still resectable. Jaundice is a symptom of extension in carcinoma of the body and tail, occurring only with liver metastases or other metastases producing common duct obstruction. Hepatomegaly with tumors of the body and tail almost invariably means liver metastases, while hepatomegaly with tumors of the head has an equal chance of representing metastases or simply biliary stasis and cholangiectasis resulting from bile duct obstruction. A palpable gallbladder associated with a tumor of the body and tail indicates metastases, since the gallbladder does not become enlarged unless the common duct is obstructed. Peripheral edema may be a presenting symptom of carcinoma of the pancreas, although it is usually a late occurrence in the course of the disease. The cause of edema is hypoproteinemia or secondary venous thromboses. Hypoproteinemia is frequent and usually a reflection of hypoalbuminemia with a relative or absolute increase in serum globulin. Blood in the feces occurs in over half of the patients with carcinoma of the pancreas. Melena may occur without extension of the tumor from its primary site by either invasion or metastases and is not necessarily an indication of advanced disease. In from 13 to 25% of patients with carcinoma of the pancreas, hyperglycemia develops.

Roentgenologic examinations rendered significant diagnostic information in 50% of the patients. Systemic venous thromboses occurred in 36.6% of patients not operated on for carcinoma of the pancreas, in 27.6% of those with carcinoma of the head, and in 50% of those with carcinoma of the body or tail of the pancreas. The median survival in those not operated on was 5 months from the onset of symptoms; palliative operations did not change this. Radical resection of the tumor increased the median survival to 12 months. Survival time, with or without operation, was not altered by the presence or absence of metastases.

Treatment of Pilonidal Sinus by Primary Closure: A Seven-Year Study. F. P. Turner and J. W. O'Neil. A. M. A. Arch. Surg. 78:398-405 (March) 1959 [Chicago].

En bloc excision, mobilization of equal musculofascial flaps of gluteus maximus muscle, and primary closure by means of removable far-and-near sutures of stainless-steel wire were carried out in 125 unselected patients with symptomatic pilonidal sinus. These patients were operated on during a 7-year period of study by 12 different surgeons. Primary wound healing was obtained in 111 patients (88.8%). Of the 61 patients operated on personally by either one of the authors, primary wound healing was obtained in 60 (98.4%). Follow-up studies were carried out in 121 (96.8%) of the 125 patients, and 102 patients were followed for more than 18 months. There were 13 recurrences, in 10.7% of the patients followed, or in 10.4% of the total number of patients operated on. If technical error could be avoided, it is believed that the recurrence rate could be held down to less than 5%. Relapses were found to occur most frequently in patients who had previously had surgical treatment by operative techniques other than the primary-closure operation, and complications of wound healing were most frequent in patients who showed evidence of acute infection at the time of admission.

The authors' enthusiasm for the primary-closure technique has continued high. This operation in their experience has provided the patient with a thin, strong, nontender scar, with minimal deformity, and a protective pad of fat and fascia over the bony prominence of the coccyx and sacrum. It is a simple operative procedure, which is applicable to the treatment of all but the most extensive lesions. It can be carried out with low morbidity and with a reasonably low recurrence rate. Wound infection can be held down to a level acceptable for any clean operative procedure, so long as satisfactory clinical judgment is exercised as to the time of surgery and so long as the surgeon is careful to obtain complete hemostasis and a meticulous wound closure.

Frozen Sections: An Evaluation of 1,810 Cases. T. Winship and R. V. Rosvoll. Surgery 45:462-466 (March) 1959) [St. Louis].

The use of frozen sections for prompt diagnosis of surgical specimens has been established as an accepted procedure in hospitals. A total of 1,810 specimens from virtually every organ of the body were frozen and studied in the department of pathology of the Washington (D. C.) Medical Center, between 1953 and 1958 to determine the percentage of accurate diagnoses with respect to specific organs. The accuracy attained for the entire series was 97.6%. For specific organs the accuracy varied between 94.3% for lymph nodes and 100% for other organs. For breasts and thyroids, the tissues most frequently examined, the accuracy was 98.1 and 96.5% respectively. A total of 43 errors were made, most of them in the first years of the study. Three false-positive diagnoses were made. A leukoplakia of the vulva was reported as in situ carcinoma, a pseudomucinous cystadenoma of the ovary was thought to be carcinoma, and a lymph node from a patient with cat scratch disease was mistaken for lymphosarcoma.

Frozen sections at the time of operation basically are indicated only when immediate additional therapeutic procedures are contemplated. In most patients no further surgical treatment will be indicated after the initial biopsy. In other patients definitive surgical treatment for cancer will follow, and in some the frozen section will prove the lesion to be inoperable. The surgeon and the pathologist must each accept certain responsibilities if the patient is to receive the maximum benefit from the frozen-section procedure. The surgeon should realize that it is the pathologist who must decide whether a given specimen can be frozen and interpreted satisfactorily or whether it would be wiser to wait for the paraffin sections. Properly employed, the use of frozen sections for establishing a diagnosis enables the surgeon to proceed with immediate therapy when indicated. The patient is spared additional anesthesia, operating room fees, and the anxiety associated with waiting for a diagnosis. Pathologists are now expected to be capable of rendering frozen-section diagnoses on tissue from any part of the body with reasonable accuracy.

Spontaneous Pneumothorax: Modern Concepts in Etiology and Treatment of an Important Syndrome in Military Practice. P. A. Thomas. Mil. Med. 124:116-130 (Feb.) 1959 [Washington, D. C.].

The author reports on 156 patients treated for 184 episodes of spontaneous pneumothorax from July, 1948, to July, 1957, at the surgical department of the Tripler Army Hospital in Honolulu, Hawaii. Sixty-one per cent of these patients were between the ages of 20 and 25 years, and 83% between the ages of 15 and 30 years. This shows an increasing prevalence of spontaneous pneumothorax among the military population served by this hospital. The etiology of spontaneous pneumothorax can no longer be considered idiopathic; multiple blebs and bullae of the lung surface have been found over the upper lobes in 15 of 19 patients in this series who underwent thoracotomy. These and other pathological changes suggest that the blebs and bullae of the lung which rupture to produce the clinical picture of spontaneous pneumothorax are secondary to an underlying peripheral pulmonary vascular ischemia. The most frequently observed symptom in the 184 episodes of acute pneumothorax was pain, which occurred in 96%; decreased breath sounds were observed in 81%, dyspnea in 60%, and hyperresonance in 61%. An uncomplicated episode of spontaneous pneumothorax is not life-endangering. However, serious complications, such as bilateral spontaneous pneumothorax, tension pneumothorax, or spontaneous hemopneumothorax, must be recognized and properly treated without delay. In this series of patients 28% were observed to have a second acute episode, and 12% had 3 or more attacks of spontaneous pneumothorax. Alternating bilateral pneumothorax occurred in 6 patients. Recurrent pneumothorax of the contralateral lung after surgical correction for the side of initial involvement occurred in 3 patients. Two patients were treated for simultaneous bilateral pneumothorax.

The best treatment today for acute pneumothorax is waterseal drainage of the pleural space with the aid of an intercostal catheter for patients with more than minimal lung collapse. The preoperative medication should include atropine or a similar drug to reduce the possible risk of a reflex-induced cardiac arrest as the parietal pleura is transgressed. All the patients in this series treated this way have received antibiotic therapy. This is rationalized on the basis that a free communication temporarily exists between the tracheobronchial tree and the pleural space with bacterial contamination. A comparison of the time required to achieve complete lung expansion by bed rest as opposed to pleural space drainage showed that the time required from the day of admission to obtain lung expansion averaged 2 weeks longer in the group of patients treated by bed rest. In conjunction with the treatment of spontaneous pneumothorax by intercostal catheter drainage of the pleural space, the author has developed and clinically tested a one-way plastic encased flutter valve to meet the military requirement for a simple, safe substitute for the waterseal trap. The primary advantage of this device is that the patient may be moved about in emergency situations. Fourteen patients in this series have been treated for an equal number of episodes of spontaneous pneumothorax by substituting the valve for the waterseal trap with satisfactory results.

Partial parietal pleurectomy has been investigated as an important component of the definitive surgical treatment for the complications of spontaneous pneumothorax. This method has proved to be an excellent method of obliterating the pleural space. It also enhances the blood supply of the peripheral lung tissue, which may be of benefit in preventing progression of pathological changes in the lung. The results have been sufficiently encouraging in this series of patients to warrant continued employment of the procedure. The results after surgery also have been encouraging. There have been no recurrences of pneumothorax on the side of operation. The longest follow-up period is now 3 years in one patient. The shortest period of observation postoperatively was 6 months. The modern approach to spontaneous pneumothorax will decrease hospital morbidity and provide a more effective utilization of manpower during periods of total mobilization.

Criteria of Operability in Malignant Arterial Hypertension. P. Mériel, F. Galinier, J. Suc and others. Semaine hôp. Paris 35:101-103 (Jan. 12) 1959 (In French) [Paris].

The authors present the various criteria which serve as a basis of indication for Smithwick's operation (lumbodorsal splanchnicectomy) with adrenalectomy in cases of essential malignant hypertension. From personal observations and hemodynamic and histological comparative investigations at the Medical Clinic of Professor Mériel at Toulouse, the authors emphasize the necessity of excluding chronic pyelonephritis and glomerulonephritis by studying glomerular filtration and renal biopsy puncture. In this way the operation will be performed only for genuine malignant nephroangiosclerosis. The ideal indication for Smithwick's operation with adrenalectomy is the case of arterial hypertension in a young person with diastolic pressure at or above 100 mm. Hg at rest, with normal glomerular filtration without glomerular and interstitial histological changes shown by renal biopsy. Renal flow should be equal to or lower than 500 cc. per minute. When glomerular filtration is below 90 cc. per minute, operation is contraindicated. The bad results which some statistics show are largely the result of the fact that patients who should not have had surgery were operated on. Operation is rather rarely indicated when all the necessary clinical and biological facts are assembled.

Tumors of the Small Intestine. R. C. Darling and C. E. Welch. New England J. Med. 260:397-408 (Feb. 26) 1959 [Boston].

Neoplasms of the small intestine are uncommon, and comprehensive reviews have usually been based on autopsy material. This report is concerned with tumors of the small intestine observed at the Massachusetts General Hospital, Boston, from 1913 to 1957. Ninety-three were found at autopsy, and 132 at operation. This study is concerned with the latter group, of which 46 tumors were benign and 86 were malignant. Nineteen of the 132 patients had no symptoms, and the tumor was first noted at operation. All except 1 of these 19 incidental tumors were benign. Of the 113 patients who had symptoms, 28 had benign and 85 had malignant tumors. Of the 85 malignant tumors, 15 were carcinoids, 32 carcinomas, 29 lymphomas, and 9 sarcomas. Symptoms of obstruction were present in 76 (67%) of the symptomatic patents, intestinal bleeding in 60 (53%), a palpable abdominal mass in the absence of intussusception in 35 (31%), and symptoms of intestinal perforation in 13 (11%). Rare symptoms included the deficiency syndrome and the carcinoid syndrome; there were also the signs of hereditary intestinal polyposis and the symptoms of multiple neurofibromatosis.

It is noteworthy that obstruction is usually chronic and intermittent. When acute obstruction of the small intestine is due to intussusception in adults, a tumor of the intestine is involved in about half of the cases, and the lesion usually is benign. Intestinal bleeding is common with all tumors except carcinoids. A palpable mass nearly always indicates a malignant tumor; when the mass is tender, a lymphoma should be suspected. Perforation is common with lymphoma and sarcoma; it is rare with cancer and was not encountered with carcinoid or benign tumors.

Eighteen of the symptomatic tumors were located in the duodenum, 48 in the jejunum, and 47 in the ileum. The cancerous lesions were most common just beyond the ligament of Treitz, and carcinoid tumors in the terminal ileum. Roentgenologic examination of the small intestine was carried out in 56 of the patients with symptoms; it resulted in the diagnosis of a neoplasm in 48 of the patients.

Forty-six benign tumors were treated, without a fatality. These tumors belonged to 5 major groups —adenomas, lipomas, myomas, fibromas, and angiomas. In the 54 patients with malignant lesions who were subjected to resections for cure before Jan. 1, 1953, 16 (30%) died postoperatively; 47% of the survivors of resection for cure were living and free of disease 5 years later.

Disruption of Muscles and Tendons: An Analysis of 1,014 Cases. S. H. Anzel, K. W. Covey, A. D. Weiner and P. R. Lipscomb. Surgery 45:406-414 (March) 1959 [St. Louis].

Of 1,014 disruptions of tendons and muscles observed in 781 patients at the Mayo Clinic between 1945 and 1954, 598 were due to lacerations and 416 were due to other causes. The average age of the patients was 40½ years, and men outnumbered women in almost all muscle-tendon groups. With respect to the anatomic distribution of the disruptions, 856 (84.4%) occurred in the upper extremities, 143 (14.1%) in the lower extremities, and 15 (1.5%) in the trunk. The large number of lacerations in the upper extremity is related to the frequency with which home, farm, and industrial accidents cause injuries about the hands and wrists. Direct injuries accounted for almost equal percentages of disruption in the upper and lower extremities, while stress rupture accounted for twice as many disruptions in the weight-bearing lower extremities as in the upper extremities. Disruptions were associated with fractures in 6.4% of cases. The flexors and extensors of the fingers, and, in addition, the musculotendinous cuff and biceps brachii, represented 76% of the disruptions in the upper extremities. The quadriceps, tendo achillis, and triceps surae (not including the tendo achillis) represented 67.8% of the disruptions in the lower extremities. Of 1,014 disruptions, 269 were partial or incomplete. Factors which probably predisposed to muscle-tendon disruption were present in 87 cases (8.7%). Tendinous calcification accounted for about 33% of the total number, as did osteoarthritis.

NEUROLOGY & PSYCHIATRY

A Clinical and Radiological Correlation of the Lesions Produced by Chemopallidectomy and Thalamectomy. G. J. Bravo and I. S. Cooper. J. Neurol. Neurosurg. & Psychiat. 22:1-10 (Feb.) 1959 [London].

The authors report on 300 consecutive patients with paralysis agitans (Parkinson's disease) who were operated on by the balloon-cannula alcohol method at the St. Barnabas Hospital for Chronic Diseases in New York and were followed up for periods ranging from 6 to 18 months. Three hundred sixty intracerebral lesions were placed in these patients and were plotted in several standard x-ray tracings of the skull. The surgical target of these lesions was the area of the globus pallidus and its efferent fibers and the ventrolateral region of the thalamus posterior to the anteroventral nucleus. The most constant and complete relief of both alternating tremor and rigidity was obtained from a lesion in the region of the ventrolateral nucleus of the thalamus. No abnormal sensory, motor, intellectual, or psychological abnormalities resulted from such a lesion. This lesion is one of choice for treatment of both tremor and rigidity. Involvement of cerebellar pathways to the ventrolateral thalamus undoubtedly contributes in some measure to the effectiveness of this lesion in alleviating Parkinsonian tremor and rigidity.

Lesions of the mesial globus pallidus, the efferent pallidal pathways, and the anteroventral thalamus provided good relief of rigidity but less consistent relief of tremor. However, in some patients tremor, which was incompletely relieved by a lesion in this complex, gradually disappeared completely within 2 or 3 months. The areas responsible for neurological complications, including motor or sensory deficits, were found to be distributed in a predictable manner, in such a way that those complications can be prevented—or when they occur be explained—in terms of the radiologic placing of the lesion.

1,000 Prefontal Lobotomies: A Five-To-10-Year Follow-Up Study. H. S. Barahal. Psychiat. Quart. 32:653-690 (Oct.) 1958 [Utica, N. Y.].

The author studied 1,095 patients, of whom 366 were men and 729 were women. This group of patients was operated on by one surgeon by a standard prefontal lobotomy method between 1946 and 1956; they all received the same postoperative care and training, and they were followed up from 5 to 10 years. Sixty-four per cent of the lobotomized male patients had been hospitalized continuously for 5 or more years at the time of operation, but only 39% of the female patients were in this category. This shows that the women were operated on earlier in their illness than the men. Of the 1,095 patients on whom lobotomy had been performed, 740 were still hospitalized at the end of the observation period, while 176 had been discharged and were still out of hospital at that time; 39 patients were in other hospitals, 85 had died, and 55 patients were lost to follow-up. Of 606 control patients, for whom permits for lobotomy could not be obtained and who were considered comparable to the patients operated on, 13 improved only enough to be discharged from the hospital. About 155 of the 176 patients on whom lobotomy had been performed, and who had been discharged from the hospital, were still well at the end of the observation period. Eleven patients who were classified as having "recovered" showed no obvious defects or residuals and returned to their former level of employment and adjustment. Of the 740 lobotomized patients who remained at the hospital, 285 showed improvement or much improvement after the operation. The remaining 455 patients showed no improvement after the operation, but it should be pointed out that they were very ill at the time of operation. None of the patients could be classified as having had their condition made worse by the operation, except perhaps those in whom convulsions subsequently developed. Of the 1,095 lobotomized patients, 68 died as a result of surgery; 20 of these patients died of convulsions from 1 month to 5 years after the operation.

The present state of psychiatry and the various complications and unfavorable features in lobotomized patients suggest that lobotomy should be limited to patients who have failed to improve after all other practical treatments, such as psychotherapy, electric shock, insulin shock, and the various ataractic drugs. The relatively high death rate, the possibilities of postoperative seizures, and the possibility of personality changes are factors to be considered carefully in every case.

The Communication of Suicidal Intent: A Study of 134 Consecutive Cases of Successful (Completed) Suicide. E. Robins, S. Gassner, J. Kayes and others. Am. J. Psychiat. 115:724-733 (Feb.) 1959 [Baltimore].

In the one-year period between May 15, 1956, and May 15, 1957, the coroners of the city of St. Louis and of St. Louis County returned a verdict of suicide in the deaths of 134 persons. In 119 of these cases the authors held a primary interview with close relatives or friends within a few weeks to a few months after the suicide. The relatives refused an interview in 13 cases, and 2 suicides were transients in St. Louis. In addition to the primary interview, interviews were obtained with other relatives, friends, job associates, clergymen, landladies, bartenders, nurses, attorneys, policemen, and physicians. A total of 305 interviews were done. General and mental hospital records, Social Service Exchange and police records were also examined.

Two striking findings were that 69% of the suicides had communicated suicidal ideas and that 41% had specifically stated they intended to commit suicide. In the majority of instances, the suicidal communications were recent (months), repeatedly verbalized, and expressed to many persons. Another striking finding was that 98% of these persons were probably clinically ill prior to their suicides. The frequency of expression of suicidal ideas was not significantly related to age, sex, marital state, religion, whether living alone or not, clinical diagnosis, occupational status, income, or education. Chronic alcoholics had a somewhat greater tendency than the other groups to make the specific statement that they intended to commit suicide. The authors point out that there is a lack of realistic information concerning what a respondent should do when confronted with this situation.

The Relationship of Epilepsy to Breech Delivery. J. A. Churchill. Electroencephalog. & Clin. Neurophysiol. 11:1-12 (Feb.) 1959 [Montreal].

Epilepsy has been known to result from cranial injury, but in the majority of epileptic patients cerebral lesions cannot be demonstrated. Patients lacking evidence of cerebral damage are said to have "idiopathic" epilepsy. On the basis of clinical and electroencephalographic (EEG) manifestations, patients with epilepsy can be segregated into 2 prominent groups: patients with focal cerebral seizures with localized paroxysmal EEG abnormalities (FCS) and patients with nonfocal cerebral seizures with diffusely distributed, bilaterally synchronized spike-and-wave EEG discharges (SSW). Patients with focal cerebral seizures (FCS) experience sensory, motor, or psychical auras of impending attacks. Some lose consciousness and behave in an inappropriately automatic fashion (psychomotor seizures). Electroencephalograms in these patients often reveal localized paroxysmal discharges. Penfield in 1954 observed atrophic and other lesions in electrically abnormal zones of cortex in a large proportion of his patients at operation. Patients with idiopathic epilepsy, that is, with nonfocal seizures, rarely have warnings of attacks, their seizures commencing with abrupt loss of consciousness; they have petit mal, myoclonic, akinetic, or grand mal seizures. Electroencephalograms in such cases often reveal bilaterally synchronous high-voltage spike-and-wave discharges (SSW).

The present report is based upon an investigation wherein the symptoms and signs of children afflicted with neurological disorders were correlated with gestational and parturitional factors. The presence or absence of neurological symptoms and signs was recorded in all patients with epilepsy, cerebral palsy, and mental deficiency examined by the author; a few had other conditions. There was a total of 706 patients ranging in age from 2 to 30 years. All but a few came from homes in the region of Detroit and were from families with good standards of nutrition and health. Neurological findings and descriptions of seizures—if any—were recorded; and the cases were classified on the basis of these manifestations into 2 main groups, one of 390 patients without and the other of 265 with epilepsy. This second group was further divided on the basis of the EEG into several subgroups.

This report is concerned particularly with the 92 patients in the first subgroup, that is, those with diffusely distributed, bilaterally synchronized high-amplitude spike-and-wave discharges (SSW). In this group with "idiopathic" epilepsy the proportion of those born in breech delivery was 19.6%, that is, it was significantly greater than the proportion of breech births (3.4%) in the general population. In contrast, the proportion of breech-born individuals (2.8%) in a group of 71 epileptic patients with localized EEG disturbances did not differ significantly from that in the general population. The proportion of breech-born in a group of (20) patients who had petit mal seizures and also in a group of (20) patients with "classical spike-and-wave" was significantly greater than that in the general population. The high incidence of breech birth in patients who have "idiopathic" epilepsy of the type associated with bilaterally synchronous spike-and-wave EEG disturbances (SSW) strongly suggests that breech delivery is an important factor in the pathogenesis of this disorder. Breech delivery does not appear to be an important factor in the origin of focal cerebral seizures.

Clinical Experience with Ataractic Therapy in Tuberculous Psychiatric Patients. R. A. Fisher and E. Teller. Dis. Chest 35:134-139 (Feb.) 1959 [Chicago].

The authors report on 235 patients with active pulmonary tuberculosis and a major psychosis, who where treated with standard antituberculosis drugs and various tranquilizing agents. The psychoses included chronic manic psychosis, depressive psychosis, chronic brain syndrome, or one of the various types of schizophrenia. The duration of the psychoses varied from 1 to 9 years. Standard antituberculosis medications included streptomycin, isoniazid, aminosalicylic acid, and occasionally viomycin. Of the 235 patients, 70 were treated with alseroxylon, an alkaloid extract of Rauwolfia serpentina, for 7 months; 68 (21 of whom had first been treated with alseroxylon) were treated with reserpine (Serpasil) for 14 months; 120 (37 of whom had first been treated with alseroxylon) were treated with chlorpromazine (Thorazine) for 14 months; and 35 are still being treated with reserpine combined with chlorpromazine. The average acceptable maintenance dose of alseroxylon was 24 mg. daily. The dose of reserpine ranged from 0.5 to 5 mg. per day and that of chlorpromazine from 150 to 900 mg. per day. Generally 1 to 3 mg. of reserpine and 75 to 150 mg. of chlorpromazine were given daily to the patients receiving combined therapy.

Results showed a definite, general, over-all improvement in both the psychiatric and the tuberculous status of the patients. In all groups there was a tendency to gain weight. Better social adjustment was seen in the patients' attitude toward accepting ward duties, helping one another, and responding to group psychotherapy. Improvement was most noticeable in acutely disturbed patients who formerly were given to frequent belligerent and combative outbursts, but to some degree all patients appeared to benefit from therapy. The percentage of psychiatric improvement was sufficient to permit psychiatric discharge of 12 (17.1%) of the 70 patients treated with alseroxylon, 27 (40%) of the 68 patients treated with reserpine, 41 (34.2%) of the 120 patients treated with chlorpromazine, and 14 (40%) of the 35 patients receiving combined treatment with chlorpromazine and reserpine. After comparing the actions of the various ataractic drugs, it was found that the combination of chlorpromazine and reserpine accomplished the beneficial effect more rapidly. Serious side-reactions were not observed.

Ataractic drugs should be considered as an adjunctive therapy in tuberculous patients with psychoneurosis. The drugs must be given in sufficient dosage and for a sufficient length of time in order to be therapeutically effective. Individualization of dosage is necessary. It should be stressed that the ataractics used in this series failed to show antituberculous therapeutic properties per se. Rauwolfia preparations should not be used in psychoneurotic patients with depressive states, as they may aggravate their depression.

Chemodectomas of the Vagal Body. E. B. Keener. Canad. M. A. J. 80:173-179 (Feb. 1) 1959 [Toronto].

The author reports on a 60-year-old woman with a chemodectoma, a tumor behind the angle of the right mandible presumably arising from the vagal body and histologically identical with tumors arising from any of the so-called chemoreceptor tissues, such as the carotid body and glomus jugulare. Twelve cases of chemodectoma of the vagal body were collected from the literature, and the case of this patient is the 13th reported on. On admission to the Montreal Neurological Institute in 1955, the patient's history revealed a 16-year duration of the tumor. She had first been treated with ultraviolet and roentgen rays in 1939, and a mass, originally diagnosed as a benign neurofibroma, had been excised in 1942. One year later a recurrence of the tumor was noted, but from 1944 to 1950 no increase in the size of the mass was noted. One year before her admission to the Montreal Neurological Institute, the patient began to have occipital pain. One month before admission, nausea and vomiting began, associated with increasing occipital pain. The patient was cachectic and spoke with a whispering voice. A firm, movable, nontender, oval mass in the right side of the neck behind the angle of the mandible extended up under the mastoid tip of the right side and into the occipital region. Roentgenograms of the skull and base revealed an enormous mass of bone destruction involving the right side of the floor of the posterior fossa, primarily around the right occipital condyle and with some involvement of the petrous process of the right temporal lobe. There was a definite active destruction of the right side of the atlas. Four days after admission the patient had a generalized seizure and after that remained unconscious until her death 5 days later.

Autopsy revealed a mass extending inferiorly to about 5 cm. from the base of the right posterior fossa, and 2 small, discrete, reddish-gray, well-encapsulated, grape-sized masses of tumor tissue were found in the right side of the submandibular region. Microscopic examination showed a neoplasm composed for the most part of oval nests containing sheets of tumor cells. The cells were usually large with a moderate acidophilic fibrillar cytoplasm and a large oval dark-staining nucleus. They were only slightly pleomorphic and had a polyhedral epithelioid appearance. No mitotic figures were observed. Chemodectomas are slowly growing and encapsulated tumors, and present a benign microscopic appearance. However, they may be extremely malignant in their gross behavior, as evidenced by local lymph node metastasis, skull invasion, and chronic compression of the brain stem. The correct management of chemodectomas arising behind the angle of the mandible consists of early diagnosis and radical excision.

Letter-Writing in a Mental Hospital. R. Sommer. Am. J. Psychiat. 115:514-517 (Dec.) 1958 [Baltimore].

To determine the relationship between letter writing and length of hospitalization, the names were secured of all patients in a mental hospital who received or sent letters during a given one-week period. There was a highly significant relationship between length of hospitalization and receiving and sending letters. The longer a patient remained in the hospital, the less likely he was to receive or send letters. Women were found to receive and send proportionately more letters than men. Patients who received letters were 10 times more likely to send letters than patients who did not receive letters. The probabilities of receiving and sending letters and receiving visitors were estimated for various durations of hospitalization. It was found that, after one year in the hospital, there is a drastic reduction in sending letters, receiving letters, and receiving visitors. Mail is undoubtedly one of the most important bridges between the hospital and the patients' homes. Letter writing should become a defined activity on the wards, as much of an activity as occupational therapy or television.

Iproniazid: Observations on Its Use in 30 Cases. R. H. Tavener. Canad. Psychiat. A. J. 4:8-13 (Jan.) 1959 [Ottawa].

Iproniazid (Marsilid) in view of its apparent effect as a "psychic energizer" was given a therapeutic trial in 17 women and 13 men, who were hospitalized for psychiatric states characterized by anergia, retardation, or lowered affect. Of the 30 patients, 4, between the ages of 45 and 48 years, had involutional depressions; 4, between the ages of 28 and 50 years, had endogenous depressions; 2, aged 62 and 64 years, had depression associated with cerebral arteriosclerosis; 1, aged 31 years, had depression associated with immature personality; and 19, between the ages of 25 and 60 years, had schizophrenia marked by withdrawal, anergia, and blocked affect. Each patient was given 50 mg. of iproniazid 3 times daily for 2 months, or until an effect was apparent; the longest duration of treatment was 8 months.

The results of treatment were as follows: Six patients were much improved, with resolution of symptoms to an extent leading to separation from hospital and resumption of previous or similar employment. Eleven were improved, with increased energy and affective response sufficient to lead to socialization in groups, participation in occupational therapy and ward management, and responsibility for personal care. Eight were unchanged with respect to their psychological and behavioral aspects. Five became worse, with increase of symptoms or behavioral disturbance leading to withdrawal of the drug. Thus, 17 of the 30 patients were benefited by the drug. The effect of the drug appeared to be a diffusely energizing one, leading to increased ability to function in social situations. The patients who appeared to respond most favorably were those with a "pure" depression, followed closely by those with the simple type of schizophrenia. The patients with addition of organic features, poor personality structure, or symptoms of hallucinations or marked bizarrerie did less well. The most disturbing side-effects, as related by patients, appeared to be dizziness, incoordination associated with tremors of the hands, and ankle edema. The side-effects necessitating withdrawal of the drug were headache, rash, and increased hallucinations.

Depressive states in patients who have not responded to other therapy, or in whom other therapy is contraindicated, appear to offer the best indication for the use of iproniazid. The use of the drug in patients with simple schizophrenia is worthy of further investigation. Side-effects with iproniazid are common, but usually not of serious import. Vitamin B supplements are advisable. Close control of the use of the drug is necessary; it should be used only by physicians with psychiatric training.

GYNECOLOGY & OBSTETRICS

Management of Swollen Arm Following Mastectomy. B. E. Brush, J. H. Wylie, J. Beninson and others. J. Michigan M. Soc. 58:216-219 (Feb.) 1959 [St. Paul].

The authors show that earlier discussions on the swelling of the arm after mastectomy stress infection as an important causal factor and mention various preventive measures. The use of constant suction drainage for several days, by the insertion of catheters at the conclusion of the operation, has reduced infection. Early arm exercises leading to free mobility of the arm and shoulder have been stressed as important in the avoidance of later arm troubles. A skin graft should be employed whenever there is any tightness of the skin flaps. Elastic arm bandages for the first 6 months after the operation have been advocated. While the authors have not used arm bandages prophylactically, their method of managing edema of the arm after mastectomy utilizes compression.

The apparatus used by the authors in the treatment of 40 patients, who had severe and disabling edema of the arm after mastectomy, has 3 features: 1. A sleeve of special fabric, in the length of which are incorporated 2 inflatable rubber tubes of about 1-in. caliber. This sleeve is laced on. A nonelastic glove is used in conjunction with the sleeve to prevent swelling of the hand while the pump is in use. 2. An electrically operated air pump with a timing device permitting inflation of the rubber tubes for 15 seconds and a collapsing rest of these tubes for 45 seconds of every minute that the device is in operation. 3. A custom-measured pressure-gradient sleeve to be worn when the pump is not in use. The authors generally begin the treatment with 3 or 4 days of rather intensive pumping. Most patients will tolerate the pump for periods of 6 to 8 hours a day. As the arm diminishes in size, the sleeve is tightened every 2 or 3 hours. When the arm has been reduced to near normal size, the sleeve is laced less tightly, and the arm is measured for the aforementioned pressure-gradient elastic sleeve. The pumping device is reapplied at intervals of a few days to a week or two and permitted to operate for several hours as needed to reduce accumulated swelling. Later, the apparatus can be used at home. Instructions for the use of the pump emphasize that it must be used under medical supervision, that its use should be discontinued if the patient experiences any distress in the arm, and that it should not be applied if there is evidence of lymphangitis.

Significant relief was obtained in all except 2 of the 40 patients. The 2 patients were in the late stages of generalized cancer and did not tolerate the device. In instances in which the edema was long-standing (7 or 8 years), the results were surprisingly good. Patients commented on the relief from discomfort and pain. The pain in most instances seemed to be due to the tension in the arm as exhibited by the hardness. Relief of pain occurred as the arm softened, and the tension decreased. A great deal of relief was obtained when the arm was only partially reduced in size. The return of the arm to a more normal state resulted in a greatly decreased incidence of lymphangitis and cellulitis. The relief from the embarrassment of a swollen arm enabled many again to lead a normal life.

Gynandroblastoma of the Ovary: Review and Report of a Case. O. R. Emig, A. T. Hertig and F. J. Rowe. Obst. & Gynec. 13:135-151 (Feb.) 1959 [New York].

The term "gynandroblastoma" was first suggested by Robert Meyer in 1930 as a name for an ovarian tumor composed of mixed elements that morphologically were compatible with both granulosa-cell tumor and arrhenoblastoma. About the patient in question he theorized that the tumor could be a hermaphroditic one, in which indifferent germinal epithelium developed into male and female gonadal components. The patient had symptoms of masculinization but also had hypertrophy of the uterus. Meyer postulated that a tumor of mixed male and female elements could produce symptoms referable to each. Since Meyer's original description several other investigators have presented cases and reviewed collections of previously reported ones. One of the authors was able to study 12 of 14 definite or questionable gynandroblastomas in the files of the Armed Forces Institute of Pathology, reaching the conclusion that 6 were bona fide gynandroblastomas. Many investigators, however, are skeptical about the existence of such a lesion. Recent classifications of ovarian tumors have either omitted gynandroblastoma or included it with question and reservation.

The history of a 59-year-old woman is presented. This patient had a tumor that was originally diagnosed as a feminizing mesenchymal tumor (granulosa-theca-cell tumor). When the sections were reviewed, the diagnosis of gynandroblastoma of the ovary was made by one of the authors without benefit of the clinical history. The features of this report appear to fit Meyer's description and prediction. The final diagnoses were chronic cervicitis; cystic and adenomatous hyperplasia of the endometrium with focal anaplasia; carcinoma in situ of the endometrium; adenomyosis uteri; endolymphatic stromal myosis; gynandroblastoma of the ovary.

A source of confusion in the literature appears to have been the inclusion of feminizing tubular tumors as gynandroblastomas. Feminizing tumors that exhibit a tubular structure without a granulosa-cell pattern fit into the arrhenoblastoma-androblastoma series proposed by Teilum. These tumors may be feminizing by virtue of the Sertoli cells according to this author. The term "gynandroblastoma" is reserved for the tumor that contains combined arrhenoblastoma and granulosa-theca-cell elements. More observations will be necessary to establish Meyer's hypothesis permanently.

Uterosacral Block. W. J. Spanos and J. C. Steele. Obst. & Gynec. 13:129-134 (Feb.) 1959 [New York].

This study is concerned with 400 parturient women in whom the autonomic nerve supply to the uterus, cervix, and upper vagina was blocked through the uterosacral ligaments. The equipment used consisted of a 6-in., 20-gauge needle, a 10-cc. Lockluer syringe, and 40 cc. of 1% Cyclaine solution. A transvaginal pudendal block was usually administered prior to the injection of the uterosacral ligaments. The advantages of the initial pudendal block were relief of pain resulting from pressure of the presenting part and relaxation of the pelvic floor muscles with, therefore, less discomfort during the injection of the uterosacral ligaments. After the pudendal block the uterosacral ligaments were injected at approximately 4 and 8 o'clock in either fornix, with the tip of the needle just below the mucosa of the vagina so as to raise a palpable wheal during the injection; 8 to 10 cc. of 1% Cyclaine was deposited on each side. The majority of women in this series received no premedication. The blocks were performed at various times during the first stage of labor and, in some instances, repeated as necessary. Cyclaine was chosen as the anesthetic solution. The essential properties possessed by this agent which make it desirable for nerve block are: (1) low absolute and relative toxicity; (2) high degree of potency; (3) short latent period; (4) prolonged duration; and (5) high degree of diffusibility.

Pain relief was excellent in 250 of the 400 women, good in 103, fair in 42, and poor in 5. Two hundred eighty successful blocks lasted for the duration of labor. The duration varied from 20 minutes to 3 hours. The majority of the blocks lasted from 60 to 90 minutes before the return of discomfort. The return of discomfort was usually dramatic and sudden rather than a gradual increase in pain. The effect (of the block) on labor was difficult to evaluate accurately. In a few the uterine motility or contraction intensity was decreased immediately after the injection; in approximately the same number the intensity of the contraction increased after the uterosacral block. In general, it was felt that the block had no beneficial or detrimental effect on the contraction intensity or frequency. There were no maternal deaths. Postpartum hemorrhages occurred in 2 women; both were due to uterine inertia. Pitocin was used in 28 women in an effort to prevent excess third-stage blood loss. Forceps were used in 14 deliveries. Of the 403 infants, 7 were lost (5 stillbirths and 2 neonatal deaths).

The combination of uterosacral block with pudendal block in labor offers a simple efficient method of securely blocking the afferent pathways from the uterus, cervix, vagina, and perineum. The anesthesia obtained is specific in its effect on the regions to be anesthetized and is limited in its actions to only those regions. The advantages of this form of anesthesia include a production of cervical softening and a lowering of the degree of lower uterine segment resistance; the woman is fully conscious, interested in the progress of her labor, and fully able to make the voluntary efforts necessary in the second stage.

PEDIATRICS

Hand-Schüller-Christian Disease: Case with Multiple Bone Defects. M. Niclós, F. Campoy and V. Arenal. Rev. españ. pediat. 14:763-782 (Nov.-Dec.) 1958 (In Spanish) [Saragossa].

A child, 20 months old, was brought for consultation by his parents. During the last 6 months he had been suffering with irregular fever and had lost much weight. Tumors on the scapular and cranial bones had appeared one after the other. The patient moaned, apparently from pain in all bones. The tumors, on palpation, were soft and gelatinous, and they did not respond to treatment with streptomycin and isoniazid. Radioscopic and roentgenologic examinations showed osteolytic bone lesions so diffuse that only the bones of the hands and of the feet were spared from lesions. There were intense hypochromic anemia, hypercholesterolemia, and hyperleukocytosis with pathological granulations of the neutrophils. The patient, however, did not have exophthalmos and diabetes insipidus, which in addition to the osteolytic lesions are characteristic of Hand-Schüller-Christian disease.

In treatment, the patient was given liver extracts, vitamin compounds, especially those of the vitamin B complex, iron, and a normal diet with moderate limitation of food rich in cholesterol. Roentgenotherapy was instituted in doses of 100 r over each focus up to a total dosage of 300 to 500 r. As a rule, one series sufficed to induce recalcification of the osteolytic lesions, but some of the lesions required the administration of a second series, which was given within 4 to 7 months after the first. The roentgen-ray irradiations were given with wave lengths corresponding to a half-value layer of 0.9 mm. Cu and with a target-skin distance of 40 cm. Great improvement was shown after 3 months of treatment. Fever disappeared, and the patient regained weight and strength. The blood became normal. The osteolytic lesions, one after another, became recalcified in the course of 2½ years. The patient was discharged as cured. A follow-up for more than 2 years thereafter showed that the clinical and roentgen-ray cure had been well sustained.

The authors conclude that roentgenotherapy should be administered early in the development of Hand-Schüller-Christian disease, for, as the disease progresses, the osteolytic lesions progress into fibrosis which does not respond to roentgenotherapy. The series of treatments should be repeated only if the osteolytic lesions are progressing at the end of a 4-to-7-month interval. The radiations should be given in the smallest possible dosage. This is to prevent disorders of the hematopoietic system, depression of articular cartilages which stops growth, and the possibility of the formation of irradiation cataracts from the roentgen-ray treatments.

Looser-Milkman's Syndrome. T. S. Sánchez. Rev. españ. pediat. 15:1-11 (Jan.-Feb.) 1959 (In Spanish) [Saragossa].

Looser-Milkman's syndrome, generally known as Milkman's syndrome, is very rare in infants, but it may occur in infants with the osteomalacia type of rickets. The disease is of unknown origin. It is characterized by the appearance of diffuse pseudofractures, with a roentgenologic aspect of multiple transparent stripes of absorption in the long and flat bones, which occur in the absence of trauma. Generally, the disease is bilateral and symmetrical. The symptoms are those of true fractures, with tumefaction and pain at the level of the pseudofractured bones and functional incapacity of the involved structures. In cases in which the osteomalacia type of rickets is controllable, the pseudofractures heal.

Several hundred roentgenograms of the thorax and of the long bones were taken during routine examination of infants on admittance to the Pediatric Hospital of the Faculty of Medicine of Seville. Only the roentgenograms of 2 infants showed the typical features of Milkman's syndrome. Both infants had the osteomalacia type of rickets and were hospitalized in critical condition. The 17-month-old infant had bronchopneumonia, and the roentgenograms of the thorax showed bilateral pseudofractures of the ribs. This patient was removed from the hospital shortly after admittance. The other infant, 19 months old, had acute tuberculosis and multifocal pneumonia, dyspnea, and cyanosis. Clinical examination and roentgenograms of the thorax and arms showed bilateral pseudofractures of the 7th and 8th ribs and, very markedly and symmetrically, of the forearms. The patient died shortly after hospitalization because of aggravation of dyspnea and cyanosis. An autopsy was not authorized.

Several factors seem to be involved in the production of pseudofractures in Milkman's syndrome. Muscular forces on the osteomalacic bones and the constant pulsation of arterial blood on the bones seem to be the main factors. This is provided that the bones are in a condition of diminished resistance to muscular action or to arterial pulsation because of the presence of avitaminosis A and of ovarian hypofunction in the mothers of the patients.

Syndrome of Acute Osteomyelitis of the Superior Maxilla in Early Infancy. H. Lieberman and J. Brem. New England J. Med. 260:318-322 (Feb. 12) 1959 [Boston].

Osteomyelitis of the superior maxilla in early infancy gives rise to symptoms and signs that may be characterized as a syndrome. While it has been described in a textbook of ophthalmology, it has received hardly any mention in pediatric textbooks. Usually, the earliest manifestation of this disease is an involvement of the orbital contents and nose, and therefore an ophthalmologist or a rhinologist may be consulted. The pediatrician or the general practitioner, not being acquainted with the syndrome, may consider the diagnosis as rhinosinusitis or conjunctivitis and miss the true nature of the underlying pathology. The authors present 2 infants with osteomyelitis of the superior maxilla, whom they observed within the past 5 years, and review the literature. The first of these 2 presented a textbook picture of this condition.

A newborn infant, usually 2 or 3 weeks of age, becomes prostrated and feverish, and swelling of one side of the face more than the other develops, with marked swelling and redness of the orbital region—so much so that the lids can hardly be opened. There is chemosis of the conjunctiva, and when the orbital contents are involved, fixation and proptosis of the globe occur. A purulent nasal discharge, most marked on the involved side, is also present. As the condition progresses, pus may appear in the nose, and fistulas may form at the alveolar process of the maxilla, at the canine fossa, or near the inner canthus of the eye on the involved side. Tooth buds may be extruded, with drainage from the alveolar process. In addition to the fever and prostration, vomiting and diarrhea usually appear. In practically all cases in which cultures have been taken, a pathogenic Staphylococcus pyogenes var. aureus has been recovered.

In both infants presented, the ethmoid sinuses were involved, and a hemolytic Staph. aureus resistant to penicillin was observed. In view of the tendency of pathogenic staphylococci to become resistant to penicillin and other antibiotics and the rising incidence of carrier rate of these organisms in hospitals, it is very likely that this syndrome will increase. Roentgenologic examination is of little diagnostic value early in this disease. Later it may show involvement of the ethmoid sinuses.

Penicillin was used successfully for the first time in this syndrome in 1945, achieving cure in 12 days. In surgically treated patients, cure usually required several months. To minimize or prevent permanent damage, early clinical and bacteriological diagnosis, surgical intervention, when indicated, and treatment with the proper antibiotic, as well as supportive therapy, are essential. Because the infection in this syndrome has a tendency to smolder, it is essential to continue with the antibiotics of choice until it is entirely eradicated.

Statistical and Biological Findings on Revaccination with BCG. G. Galzerano and R. Sorrentini. Arch. tisiol. 13:1139-1151 (Dec.) 1958 (In Italian) [Naples].

Most of the 5,479 children who were vaccinated with BCG became and remained tuberculin reactors for a period of 4 years. Follow-up inspection during this period demonstrated, though, that the number of tuberculin nonreactors began to increase. Revaccination with BCG was administered intradermally in doses of 0.10 cc. to 340 children; 184 of these were nonreactors to the first tuberculin test, and 154 were initially tuberculin reactors but subsequently became insensitive to the tuberculin test. Failure to develop reaction to the tuberculin test on first vaccination was attributed to the erroneous (too low) dosage of BCG vaccine. Of revaccinated children, 85 became tuberculin reactors. A higher rate of tuberculin nonreactivity was thus observed among the revaccinated children than among those who were vaccinated only once. It was possible to develop a reaction to tuberculin in 31 children by repeating the vaccination 2 or 3 times. There seemed to be a familial feature of tuberculin nonreaction in this series of vaccinated children, because of 19 children, who were revaccinated twice, 6 were brothers belonging to 3 different families.

Duodenal Ulcers in Children. H. P. Jackson and M. Westrope. South. M. J. 52:147-150 (Feb.) 1959 [Birmingham, Ala.].

The 9 children with duodenal ulceration described in this paper ranged in age from 10 months to 8 years. Their cases were collected in a period of 3 years from a group practice of 4 pediatricians. Only patients with roentgenologic evidence of an ulcer crater or a niche were included, since the less definitive symptoms of pain, vomiting, melena, and hematemesis are nonspecific, although contributory. All films were reviewed independently by at least 2 competent roentgenologists. The children were somewhat younger than those in other reports, but this probably reflects the concentration of younger children in this particular practice. The male preponderance of 7 to 2 is compatible with the adult ratio of 4 to 1. The family history was positive in one-third of the children. Abdominal pain was the commonest presenting complaint, being present in 6 of 9 patients. The pain was poorly defined. In 3 cases it was relieved by food, but in 2 instances it seemed to be made worse by eating. No relationship to meals could be established in the other 4 children. The pain was usually of short duration. Night pain was a symptom in only one child, who seemed to have the adult type of ulcer. Bleeding occurred in 2 patients and in each was severe as well as sudden in onset. Vomiting was present in only one patient, but in other series it seems to be more characteristic, especially of the older children.

All the children treated responded promptly to frequent feedings of bland foods. Antispasmodics were not necessary to relieve symptoms, and antacids were not used. Effort was directed toward relieving emotional stresses of these children. The nature of such stresses acting on these children and their reactions to them are being investigated. It is believed that the diagnosis of duodenal ulceration is often missed in children.

Listeria Meningoencephalitis in Children. H. H. Bassøe, E. Glück and T. Mork. Nord. med. 61:184-185 (Jan. 29) 1959 (In Norwegian) [Stockholm].

Of 73 bacteriologically verified cases of Listeria meningitis or meningoencephalitis published up to 1956, 32 were in children, aged under 14 years. The clinical picture in meningoencephalitis due to Listeria monocytogenes does not differ from that in other suppurative meningitides but can in rare cases simulate serous meningitis. The diagnosis is bacteriological. The resistance of Listeria meningoencephalitis to antibacterial agents varies. In every case determinations of resistance in vitro are necessary. In the fatal case described, in an infant, aged 19 months, the microbe strain showed all characteristics of L. monocytogenes. Treatment with massive doses of penicillin, sulfonamides, and streptomycin was apparently without clinical effect. The purulent process was established by microscopic examination on autopsy. Grave cerebral edema caused tentorial herniation and necrosis of the uncus hippocampi.

Current Treatment of Whooping Cough in Nurslings and Small Children. J. Marie, G. Sée and M. Gaiffe. Rev. immunol. 22:432-455 (July-Sept.) 1958 (In French) [Paris].

The authors report on 1,621 nurslings and children, aged less than 5 years, with whooping cough who were treated at the Children's Hospital in Paris between 1941 and 1957. Of the 1,621 patients, 1,051 (group 1) were treated between 1941 and 1946, 286 (group 2) were treated between 1950 and 1952, and 284 (group 3) were treated between 1955 and 1957. Of the patients in group 1, 109 died, representing a mortality rate of 10.38%; 11 of the patients in group 2 died, representing a mortality rate of 3.84%; and 4 of the patients in group 3 died, representing a mortality rate of 1.40%. This significant improvement in the mortality rate is considered to be the result of 3 factors, namely, administration of antibiotics (such as chloramphenicol and streptomycin) and hyperimmunized human gamma globulins, use of active sedatives (such as promethazine and phenobarbital), and nursing adapted to the needs of the patients, including the use of an aspirator, maintenance of correct aeration, administration of oxygen after severe paroxysms, and providing an adequate caloric ration by small fractionated meals. In addition to the improved mortality rate, the number of paroxysms of cough has been reduced, and the asphyxiating character of the paroxysms has rapidly disappeared. This has resulted in a definitely more favorable prognosis of whooping cough in hospitalized nurslings and small children.

Acute Bacterial Meningitis in Children: Review of 379 Cases Treated from 1945 to 1957. J. Kauhtio, M. Paatela and I. Rantasalo. Nord. med. 61:177-180 (Jan. 29) 1959 (In Swedish) [Stockholm].

Acute bacterial meningitis is considerably more common in infancy than later. One-fourth of 379 children with acute bacterial meningitis who were treated from 1945 to 1957 were under 3 months of age; two-thirds were under 1 year. On admission, the presence of meningitis had been suspected in only about half the cases. Early diagnosis with adequate treatment is of the greatest importance for the prognosis. Of the 111 deaths, one-third occurred during the first 24 hours after admission. The mortality was highest in the infants aged less than 2 weeks when the disease set in. In general, symptoms of circulatory collapse dominated the picture. The first measures must be directed to overcoming the condition of shock. Neisseria meningitidis was the causal organism in 21% of the cases, Streptococcus pneumoniae in 20%, and Hemophilus influenzae in 29%; other bacteria were met with in 14%, and in 59 cases the bacteria were not demonstrated but the diagnosis was considered certain. In Neisseria meningitis the standard treatment was with sulfonamides alone or in combination with penicillin, but good results were also attained with other antibiotics, perhaps especially chloramphenicol. The treatment rarely had to be continued for more than 5 to 7 days. In Str. pneumoniae meningitis massive doses of penicillin were effective. The medication should be applied with gradually diminishing doses for fully 3 weeks to eliminate the danger of recurrence. In the H. influenzae cases the best results were seen with chloramphenicol. From 7 to 10 days' treatment seemed to suffice. This treatment proved the most effective in the cases with unidentified bacteria also. Intrathecal administration of antibiotics in acute bacterial meningitis was not applied after 1951.

A New Syndrome of Multiple Malformations: Skeletal Malformations of the Neck and Hands, and Presence of a Dystopic Solitary Kidney. M. L. Grossi-Bianchi and R. Bruni. Minerva pediat. 10: 1457-1463 (Dec. 8) 1958 (In Italian) [Turin, Italy].

A girl, 11 years of age, was hospitalized for episodes of pain in the vertebral column and for afternoon headaches that had persisted for 1½ years before admission. A short neck with low hair line, stubby hands and feet, brachydactyly with very short little fingers, hypotrophic muscles of the right arm, difficulty or occasional inability in flexing the fingers, slight mental deficiency, stammering, and nocturnal enuresis were the anomalies either reported on or observed on inspection at the time of admission. Objective examination disclosed enlargement of the liver, slight enlargement of the heart, slight hypertension, and hypersomia.

Roentgenologic examination of the skeleton demonstrated a slight degree of diffuse osteoporosis, scoliosis in the cervical region, partial fusion between the 3rd and 4th and between the 6th and 7th vertebrae, an excessive number of bilateral cervical ribs, and structural changes of the upper ribs and upper vertebrae. The structure of the skeleton indicated hypersomia in the sense that this 11-year-old girl had the skeletal structure of a girl of 12 or 13 years. Renal arteriography revealed the presence of a solitary kidney abnormally situated in the region of the sacrum. Examination of the eyes revealed no anomalies. The functional tests of the solitary kidney revealed a disorder of the tubular function, but there was no sign of renal insufficiency. A pelviopneumoperitoneum indicated the probable existence of only one ovary. The case of this patient is most close to the clinical description of the Klippel-Feil syndrome.

DERMATOLOGY

Algerian Ivy Dermatitis: A California Disease. C. S. Dorsey. California Med. 90:155-159 (Feb.) 1959 [San Francisco].

The author describes the dermatitis caused by Algerian ivy in 12 persons. Two of these cases had been reported previously. Algerian ivy is largely cultivated in California, and dermatitis was produced in almost all these persons within 24 to 48 hours after trimming the plant. Although Algerian ivy is not even distantly related to poison oak or ivy, the eruption caused by the sap of Algerian ivy is similar to, but milder than, that produced by poison oak. The sites most frequently involved in this series were the dorsal surfaces of the hands, the volar surfaces of the wrists, the face, and the periorbital regions. The degrees of inflammation ranged from mild to moderately severe. In contrast to dermatitis caused by poison oak, these patients had no eruption on the genitals.

Effective results were obtained in this series only with the administration of corticosteroids. A daily dose of 20 mg. of prednisone given orally was usually sufficient to reduce dermatitis to a tolerable level within 2 or 3 days of treatment. In a few patients, however, it was necessary to repeat the initial dosage of 20 mg. daily for 7 to 10 days to control dermatitis. As soon as the symptoms began to disappear, the initial dose was gradually diminished by 2.5 mg. daily. It is emphasized that the decrease in dosage should be carried out slowly and carefully. No favorable response was obtained in one patient with the oral administration of prednisone, but the symptoms disappeared after corticotropin gel injections. Topical treatment was not effective in any patient. Algerian ivy does not cause dermatitis on first contact; repeated exposures are needed to induce an allergic response.

Twenty Years of Yaws Treatment Amongst Aboriginals in South Orissa. A. R. S. Macdonald. J. Christian M. A. India 34:26-30 (Jan.) 1959 [Calcutta].

Although Manson in his textbook on tropical diseases describes yaws (treponematosis, or frambesia tropica) as rare in India and China, in certain areas of India it is frequently seen, especially among aboriginal tribes. In the south of Ganjam district, Orissa, 50 miles inland from the east coast and 400 miles southeast of Calcutta, lives an aboriginal tribe, the Saoras, who number about 200,000. Dr. J. H. West, the predecessor of the author at the Mission Hospital of Ganjam district, first observed the disease among the Saoras in 1924 and recognized it as yaws in 1930. Arsenicals, such as neoarsphenamine, were used for treatment from that time until 1948-1949. Since then penicillin preparations have been given by injection. At present the author uses benethamine penicillin G or a combination of potassium penicillin G, procaine penicillin G, and benzathine penicillin G intramuscularly. Because of the dramatic response of yaws to either neoarsphenamine or penicillin, the patients rarely return even for a second injection.

In the past 20 years a total of 8,309 patients with yaws were treated at the hospital. To illustrate some of the aspects of the disease among the Saoras, the author tabulated data on 487 patients for whom accurate records were available. Since the World Health Organization has classified yaws into 9 groups, the former classification of yaws into primary, secondary, and tertiary lesions is no longer used. Lesions are referred to as either early or late. The primary lesion of yaws was formerly referred to as mother yaws or frambesia. A list of the locations of the primary lesion of yaws in the 487 patients showed a predilection for the lower limb (278 patients, 57.3%). The back of the trunk and the scalp were rarely involved. An abrasion or small ulcer often antedated the primary lesion of yaws. The author believes that frequently minute flies carry the spirochete from one person to another, since an investigator in Jamaica has produced evidence that Hippelates papillipes, a tiny fly, carries the yaws spirochete from yaws lesions to ulcers or breaks in the skin of previously uninfected persons. At the author's hospital several initial yaws lesions were seen implanted on the sites of recent vaccination.

The early lesion of cutaneous yaws, the frambesioma, is a papillomatous lesion. These papillomas were not observed on mucosal surfaces, but they were common, especially in children, at the squamomucosal junctions (lips, external nares, anus, vulva) and in moist areas, such as axillas, anal cleft, inguinal regions, and beneath pendulous female breasts. Nearly always more than one area of the body is affected at one time by papillomas. The incidence of papillomas in various parts of the body of the 487 patients was tabulated, but the incidence of other lesions of early yaws, such as papules, macules, plaques, and nodules, was not studied. Squamous macular and hypertrophic macular lesions of the palms and soles were seen in 86 cases. Many of these were painful and persisted or recurred over many months. Periostitis and osteitis were seen frequently, with intense rheumatic pains, especially related to the large joints—knees, ankles, elbows, shoulders—and also to the joints of the hands and feet. The most characteristic lesion of late yaws was ulceration. Latent yaws, in which no active lesions are present but the patient is seroreactive to serologic tests for syphilis, may occur early or late. Relapses are common.

Does Serum Gonadotrophin Cure Acne Vulgaris? J. H. S. Pettit. Brit. M. J. 1:557-558 (Feb. 28) 1959 [London].

Serum gonadotropin was used in treating 29 male and 20 female patients with acne vulgaris. Of these patients, those with mild cases had been receiving routine treatment with 1% cetrimide as a degreasing application and a mild exfoliative lotion, those with more severe cases had been receiving ultraviolet light irradiation, and those with the most severe cases had been receiving 250 mg. of tetracycline daily for 3 weeks out of every 4. All these patients were then provided with tablets labeled A or B and asked to cooperate in an investigation to test the efficacy of a new drug. The course of treatment was for 12 weeks, and at the end of every 4 weeks each patient was seen and requested to assess whether the additional treatment had increased the effect of the one previously given. The actual course of treatment varied from month to month, and the patients took 2 tablets a day for the first 4 weeks, 1 daily for the next 4 weeks, and then 1 every alternate day for the rest of the trial. Throughout the investigation neither the patients nor the physician knew which tablets contained serum gonadotropin and which were placebos. It was not until this report was completed that it was disclosed by the manufacturers that the B tablets contained the serum gonadotropin. The course was 100 units daily for 4 weeks, 50 units daily for the next 4 weeks, and 50 units on alternate days for the final 4 weeks.

So far as can be ascertained, all the patients allowed the tablets to dissolve in the mouth and so absorbed the drug transmucosally. Six men and 3 women failed to complete the course; in none of the defaulters was this failure due to adverse effects of the drug. Of the remaining 40 patients, 21 received tablet A and 19 patients received tablet B. Nine (42.9%) of the 21 patients and 8 (42.1%) of the 19 patients thought that the addition of the tablet had enhanced the speed of improvement, while 9 (42.9%) of those receiving tablet A and 9 (47.4%) of those receiving tablet B noticed no change either way. Three of the 21 patients and 2 of the 19 suffered a definite deterioration during the 3 months. There was, therefore, no evidence whatsoever from this trial that the patients derived any benefit from the treatment. The uncontrolled trials reported in France and England have not been confirmed, and acne vulgaris remains a condition for which there is no known cure.

OPHTHALMOLOGY

Results of Resection of the Levator Muscle Through a Skin Incision in Congenital Ptosis. R. N. Berke. A. M. A. Arch. Ophth. 61:177-201 (Feb.) 1959 [Chicago].

According to Berke most ophthalmologists believe that resection of the levator muscle gives the best cosmetic and functional results in blepharoptosis. This study is concerned with 147 operations for resection of the levator through a skin incision. Of the total number, 111 were unilateral and 36 were bilateral operations; 108 were primary procedures and 29 secondary. At the time of operation the youngest patient was 14 months and the oldest 32 years; the average age was 6 years 3 months. The external method for resection of the levator was better than the internal operation in congenital ptosis, because (1) it produced a greater amount of correction and (2) the operation was easier for the surgeon. The external method gave a greater amount of correction, because more levator tissue could be excised and the levator was advanced on the tarsus.

The survey of the 147 external operations showed that (*a*) final overcorrection was the rule in the presence of good levator action unless the ptosis was undercorrected at the time of operation, (*b*) final undercorrection was the rule in the presence of poor levator action unless the ptosis was overcorrected at operation, (*c*) overcorrection of the ptosis on the operating table was impossible when the levator muscle was too thin to support the lid adequately, and (*d*) a second resection of the levator gave a high percentage of satisfactory results only when the levator action was good. Full correction of the ptosis was obtained in over 70% of the cases by the external operation whenever (*a*) the ptosis was undercorrected on the table 2 or 3 mm. in the presence of 10 to 12 mm. of levator action, (*b*) the ptosis was fully corrected and the levator action was 7 mm. in amount, and (*c*) the ptosis was overcorrected 2 to 3 mm. and the levator function measured less than 4 mm.

Amaurosis Congenita (Leber). J. Schappert-Kimmijser, H. E. Henkes and J. van den Bosch. A. M. A. Arch. Ophth. 61:211-218 (Feb.) 1959 [Chicago].

The authors call attention to a type of congenital blindness first described by Leber in 1869, classified by him as belonging to the tapetoretinal degenerations with amblyopia, and designated as amaurosis congenita. Leber also stressed the high incidence of hereditary factors in this eye lesion. Recent reports from other European countries on certain eye defects fit in with Leber's description. One of the authors was able to collect 227 cases of amaurosis congenita (Leber); 114 of the patients were adults and 113 were children. Of the latter, 109 were blind and only 4 were partially sighted (blindness was defined as a vision of 1/10 or less; vision of the partially sighted was up to 1/4). The material was collected in the course of an investigation into the causes of blindness in the Netherlands. The number of blind children registered so far seems to be fairly complete; it is considered to be approximately 600. The percentage of this disease in the general population of known blind persons (adults and children together, approximately 6,000) is 3.8%, whereas in children the authors calculated an incidence of 18%. The data of the 227 cases under discussion were submitted by a large group of Dutch ophthalmologists. Various diagnoses were made; the most frequently found were the following: (1) connatal amaurosis of unknown origin (probably centrally located, e. g., cerebral hemorrhage during delivery); (2) diffuse chorioretinitis (congenital syphilis?); (3) atypical tapetoretinal degeneration, e. g., retinitis pigmentosa sine pigmento; and (4) connatal optic atrophy.

The authors confined their studies to the children. Fifty-six were examined, and electroretinograms were obtained. The characteristic symptoms of this form of congenital amaurosis are: (1) connatal amaurosis or greatly impaired vision; (2) a marked discrepancy between the fundus picture and the visual function; (3) a recessive heredity; and (4) a reduced electrical activity of the retina, in that electroretinography reveals either complete absence or greatly reduced photopic activity of the retina. Nystagmus or nystagmoid eye movements are observed in the majority of patients. Photophobia is also occasionally observed. The incidence of cataract and keratoglobus is greater in older persons.

The recessive autosomal character of amaurosis congenita (Leber) was made clear by the pedigree chart of a family in a Dutch isolate which included 13 cases of this condition. The demographic history of the people of this isolate, an island not joined to the mainland until 1941, indicated that the present population of about 4,000 can be regarded as the progeny of at most 75 marriages after the plague of 1637. The mean coefficient of inbreeding in this population must be extremely high, and the disease is of heredofamilial character.

Chronic Progressive External Ophthalmoplegia: Report of a Case with Histopathologic Examination of External Eye Muscle and Skeletal Muscle. B. Nicolaissen and A. Brodal, A. M. A. Arch. Ophth. 61:202-210 (Feb.) 1959 [Chicago].

A number of investigators who have described the histological findings made in the external eye muscle in biopsies or autopsies on patients with chronic progressive external ophthalmoplegia agree that the changes are of the type usually seen in skeletal muscles in progressive muscular dystrophy. They are of the opinion that chronic progressive external ophthalmoplegia is closely related to progressive muscular dystrophy and represents a particular type of this disease with preponderant or selective affection of the extrinsic eye muscles. In this paper the authors present a woman, aged 53 years, in whom the history and the clinical findings demonstrated that the diagnosis of chronic progressive external ophthalmoplegia was justified. Her symptoms started at the age of 47, and in the course of a few years a complete external ophthalmoplegia developed. The excretion of creatine and creatinine in the urine showed no significant changes.

Biopsy of the right external rectus muscle showed histological changes similar to those found in muscular dystrophy: increase of connective tissue, even within the primary muscle bundles: atrophy of muscle fibers without grouping of fibers in the same stage of atrophy; granular "degeneration" of the sarcoplasm in some fibers with loss of myofibrils; and changes in the nuclei of the muscle fibers. Biopsy of the sternocleidomastoid muscle showed similar but less marked changes of the same type. The histological findings were in agreement with the view that chronic progressive external ophthalmoplegia may be a particular form of muscular dystrophy. The authors feel, however, that it would be premature to conclude that all cases diagnosed clinically as chronic progressive external ophthalmoplegia are of the myopathic type.

THERAPEUTICS

Treatment of Pernicious Anemia by Oral Administration of Vitamin B_{12} Without Added Intrinsic Factor. E. A. Brody, S. Estern and L. R. Wasserman. New England J. Med. 260:361-367 (Feb. 19) 1959 [Boston].

The authors studied 17 patients with megaloblastic anemia, of whom 14 had pernicious anemia, 2 had undergone total gastrectomy, and one presented the malabsorption syndrome. Each patient received vitamin B_{12} tablets (50 mcg. each tablet) 3 times daily for periods of 2 to 34 months. No supplementary intrinsic factor was given. Each patient exhibited a good response, both symptomatically and hematologically. Complete remissions occurred in 11 patients with pernicious anemia, in one patient who was subjected to gastrectomy, and in one patient with the malabsorption syndrome. Responses to the therapy in the remaining 4 patients were excellent but not optimal. The average time elapsed between initiation of therapy and complete remission was 3.7 months.

Maximal reticulocytosis occurred on the 5th to the 14th day after starting therapy, and counts ranged from 5.4 to 42.8%. Macrocytosis was present initially in all patients except one, but the red blood cells became normocytic before the maximal hematocrit was reached in 12 patients and after the maximal hematocrit was reached in the remaining 5 patients. Prompt reversion of megaloblastic to normoblastic erythropoiesis occurred within days after the start of therapy. Leukopenia was present in 5 patients with pernicious anemia, in one patient who underwent gastrectomy, and in the patient with the malabsorption syndrome. After therapy was begun, prompt reversion to normal occurred in all these patients except one. In 5 patients with thrombocytopenia normal platlet counts were reached after therapy. In 6 patients neurological symptoms were present; these disappeared or were partially corrected by therapy in 5 patients and remained unchanged in the 6th. Levels of serum vitamin B_{12} remained subnormal in 12 patients.

When 50 mcg. of vitamin B_{12} is administered orally to a patient lacking the intrinsic factor, only a small percentage is absorbed. Nevertheless, when the drug is administered 3 times daily for a certain period, this quantity is apparently sufficient to effect a complete hematological remission and to improve the neurological status of most of the patients. The reticulocyte response in the patients of this series was somewhat delayed in its appearance, but the height of the response was comparable to that expected with therapy given parenterally. It is suggested that patients with pernicious anemia receiving vitamin B_{12} orally be followed closely by appropriate hematological studies, since the tissue reserves of vitamin B_{12} are never very high. When a rapid response is essential, therapy should be given parenterally. The results of this study confirm the concept that the absorption of large doses of vitamin B_{12} is not dependent on the presence of intrinsic factor.

Peroral Treatment of Diabetes. H. Kjørstad. *Tidsskr. norske lægefor. 79:55-58 (Jan. 15) 1959 (In Norwegian)* [Oslo].

From August, 1956, to August, 1958, 48 selected patients (17 men and 31 women) with diabetes were given peroral medical treatment. The disease had been diagnosed recently in 21 patients; the others had had diabetes for an average of 6 years; 6 patients had used insulin for more than 2 years. The patients were hospitalized for a control period of 1 or 2 weeks before the start of the treatment. The first 31 patients received carbutamide; from October, 1957, on all new patients were given tolbutamide, and from the spring of 1958 on only tolbutamide was given. The carbutamide dosage was usually 2.5 Gm. daily until effect appeared or the treatment was ended. The tolbutamide dosage was 3 Gm. the first day, 2 Gm. the second day, then 1.5 Gm. daily until there was effect; in a couple of cases the dosage was 3 Gm. daily till effect was seen. Control examinations, usually ambulant, were carried out after 1 or 2 weeks, then at 2-to-4-month intervals. The criteria for primary effect of the treatment were definite fall in the fasting blood sugar, preferably to 150 mg. per 100 ml. or lower, urine free from sugar or containing only small amounts, and disappearance of every tendency to ketonuria. In one instance carbutamide was withdrawn after a day because of vomiting and fever, and in 8 cases the treatment was stopped because of lack of effect. In 4 cases treatment with carbutamide was discontinued because of side-effects. In 4 cases peroral treatment was discontinued because of failure, which developed after from 12 to 24 months. During the time of treatment 3 patients died of causes unrelated to the diabetes. In 6 patients, all well regulated with relatively small dose, the attempt was made to discontinue the medication after treatment of 8 to 18 months; in 3 patients the treatment was resumed because of definite aggravation after 4 to 6 weeks, and the other 3 patients have to date carried on without medication for from 3 to 6 months. Of the original 48 patients, 25, observed for from 1 month to 2 years, are continuing the peroral treatment.

Caution in peroral treatment of diabetes is necessary. It has not been disproved that secondary degeneration of the B cells in the pancreas with aggravation of the basic disease may occur on long-continued peroral treatment; there is the question of possible development of vascular, late diabetic manifestations; and, finally, the patients are not protected in intercurrent conditions with acute aggravation of the diabetes. Patients for whom the tolbutamide treatment is to be tried should not have developed the disease before the age of 40 to 45 years, should not have used insulin for a longer time, and should be without any tendency to acidosis or coma. In a group of patients selected along these lines, the treatment will fail primarily in 15 to 30%. Tolbutamide is contraindicated in hepatic diseases, renal insufficiency, diseases of the thyroid gland, and pregnancy. A large part of the diabetic clientele will fulfill the conditions named, but insulin remains the sovereign medicament, and the tablet treatment is reserved mainly for those patients for whom insulin therapy presents special inconveniences.

Liothyronine in the Management of Obesity. C. Ressler. New York J. Med. 59:615-621 (Feb. 15) 1959 [New York].

The synthesis of liothyronine (Cytomel) induced the author to reevaluate thyroid therapy for obesity. At an endocrine clinic in Bellevue Hospital, New York, he conducted a clinical comparison of liothyronine with a placebo. All obese patients referred for weight reduction were interviewed, examined, and laboratory tests were made, including urinalysis, complete blood cell count, serology, and tests of serum cholesterol, basal metabolism, and 24-hour radioiodine (I^{131}) uptake. Patients were also examined for clinical evidence of heart disease or evidence of myocardial damage as demonstrated by electrocardiograms. All patients were placed on a well-balanced 1,100-calorie diet. Thirteen received 50 to 75 mcg. of liothyronine daily; another 13 patients received a placebo. All patients thought they were receiving active medication. They were seen at 2-week intervals, and subjective symptoms and reactions were noted. Records were made of body weight, pulse, and blood pressure. The study lasted for more than a year. The serum cholesterol and basal metabolism were tested before the termination of the study.

Patients who received the active drug lost a total of 123½ lb. (56 kg.), an average weight loss of 9½ lb. (4.3 kg.). Patients who received the placebo gained a total of 35½ lb. (16.1 kg.), an average weight gain of 2 7/10 lb. (1.2 kg.). This statistically significant difference emphasizes the appreciable weight loss obtained with the use of liothyronine. This was accomplished without troublesome side-effects and without objective evidence of more than slight elevation of the metabolism. Liothyronine was found to be a useful drug in effecting a slow stabilization of weight at a lower level in obese patients.

A Five-Year Assessment of Patients in a Controlled Trial of Streptomycin with Different Doses of Para-Aminosalicylic Acid in Pulmonary Tuberculosis: Report to the Tuberculosis Chemotherapy Trials Committee of the Medical Research Council. W. Fox and I. Sutherland. Quart. J. Med. 28:77-95 (Jan.) 1959 [London].

In 1949 a joint subcommittee of the Medical Research Council and the research committee of the British Tuberculosis Association planned a controlled clinical trial of streptomycin with different doses of *p*-aminosalicylic acid (PAS) in the treatment of pulmonary tuberculosis. Patients with acute extensive disease were allocated at random to 3 series. All the patients received 1 Gm. of streptomycin daily for 3 months, in combination with sodium salt of PAS in dosages of 20, 10, or 5 Gm. daily; the 3 series were referred to as SP 20, SP 10, and SP 5. Results from a 6-month observation were published in 1952. The progress of the 3 groups was similar in all the clinical and roentgenologic assessments. There were, however, important differences between the groups in the incidence of streptomycin-resistant strains of bacteria, the proportion being least for the patients receiving 20 Gm. of PAS (sodium) daily, and greatest for those receiving 5 Gm. of PAS (sodium) daily. The present report gives the results of a follow-up of the 3 series of patients for a period of 5 years after admission to the trial. It represents a study parallel to the 5-year assessments of the 2 earlier Medical Research Council controlled trials of streptomycin and PAS in pulmonary tuberculosis.

This report is concerned with 115 young adults, ranging in age from 15 to 30 years, who had acute, progressive, bilateral pulmonary tuberculosis, believed to be of recent origin, bacteriologically proved, and unsuitable for collapse therapy, a particularly grave form of tuberculosis. On entry to the trial there were more patients severely ill in the SP 10 series, and fewer in the SP 5 series, than in the SP 20 series. After the first 3 months there were slight differences in subsequent treatment, which probably reflect the differences in the initial clinical condition of the patients in the 3 series. About two-thirds of the patients had some form of collapse therapy or resection during the 5 years; about two-thirds received further chemotherapy, for an average duration of just under 8 months, usually in several short courses.

By the end of 5 years 19% of the SP 20, 26% of the SP 10, and 21% of the SP 5 patients had died; 66% of the SP 20, 45% of the SP 10, and 62% of the SP 5 patients had quiescent or arrested disease. The less satisfactory results in the SP 10 series are probably a consequence of the initial clinical differences. By the end of the first 6 months 15% of the SP 20, 35% of the SP 10, and 52% of the SP 5 patients were found to harbor streptomycin-resistant strains of bacilli; these differences were not reflected in the outcome over the 5-year period. The outcome of the disease was less favorable in patients who had extensive cavitation, high pyrexia, or a high erythrocyte sedimentation rate, on admission to the trial. It was also less favorable in patients who failed to improve roentgenologically, who remained bacteriologically positive, or in whom the temperature or sedimentation rate failed to respond at the end of 3 months.

Nephrotic Syndrome After Application of Mercurial Diuretics. W. F. Christiansen. Ugesk. laeger **121:** 200-204 (Feb. 5) 1959 (In Danish) [Copenhagen].

The cases of four patients with the nephrotic syndrome which developed after treatment with mercurial diuretics are described. Autopsy was performed in the 3 fatal cases. Microscopic examination of the kidneys excluded the possibility of thrombosis of the renal veins, glomerulonephritis, amyloidosis, diabetes mellitus, collagenoses, and myelomatosis as causes of the nephrotic syndrome. The 4th case was regarded as a toxic nephrosis. The nephrotic phenomena were ascribed mainly to glomerular changes, even though the tubular changes were more manifest in the microscopic preparations.

Peripheral Effect of a Thioisobutyric Derivative of Methylthiouracil. E. Arrigoni-Martelli and M. Kramer. Atti Soc. Lombarda sc. med.-biol. 13:273-275 (no. 3) 1958 (In Italian) [Milan, Italy].

The peripheral effect of MOPTI (4-methyl-6-oxypyrimidin-2-thioisobutyric acid) and of methylthiouracil (MTU) to block or reduce oxygen consumption in albino male rats treated previously with thyroxin was studied. The effect of MOPTI on the oxygen consumption became evident only when a dose of 400 mg. per kilogram of body weight was given and became more marked when the dose was increased to 600 mg. per kilogram. The oral administration of the drug was less effective than the parenteral. A dose of MTU of 200 mg. per kilogram markedly depressed the metabolic rate. A second group of rats were then given a subcutaneous dose of thyroxin, 1 mg. per kilogram of body weight, for a period of 10 days. This caused a marked increase in metabolic rate. Administration of a dose of MOPTI of 400 mg. per kilogram after treatment with thyroxin caused a drop in the metabolism within 10 days; the values were only 30% higher than those in rats of the contratest group, and the metabolism dropped by 26% after 20 days. A dose of MTU of 150 mg. per kilogram had an immediate effect similar to that of a dose of MOPTI of 400 mg. per kilogram, but after 20 days of treatment the oxygen consumption of rats treated with MTU was still 28% higher than that of rats of the contratest group. In a third experiment a dose of thyroxin of 1 mg. per kilogram of body weight and a dose of MOPTI of 400 mg. per kilogram were administered contemporaneously, and the metabolic rate remained within normal values. Contemporaneous treatment with a dose of MTU of 150 mg. per kilogram and a dose of thyroxin of 1 mg. per kilogram proved less effective; at the end of the experiment, in fact, oxygen consumption was 40% higher than the mean normal values.

Hypotensive Agents. A. R. Krogsgaard. Nord. med. 61:123-131 (Jan. 22) 1959 (In Danish) [Stockholm].

Reserpine causes sedation and reduction in blood pressure mainly by central effect, but satisfactory results are attained in only a small number of patients. When it is applied in combination with ganglion-blocking agents and hydralazine, though, reserpine has considerable value. Because of the risk of depression, the dose of reserpine must be kept at about 0.5 mg. daily, and its administration should be avoided in patients predisposed to depression. Hydralazine causes a fall in blood pressure by direct peripheral vascular effect and, to a less degree, by central effect. The hypotensive effect is moderately strong. The minute volume rises, and caution is required in patients with angina pectoris and heart insufficiency. Side-effects at the start of treatment can often be counteracted by giving reserpine simultaneously and by careful dosage. Because of the risk of late toxic symptoms, the daily dosage should be 400 mg. at the most. Applied with reserpine, hydralazine is adequate in most cases of benign hypertension; in malignant hypertension it is often a valuable supplement to treatment with ganglion-blocking agents. Ganglion-blocking agents are the most powerfully acting hypotensive substances. In dosage attention must be paid to the orthostatic fall in blood pressure. The side-effects, of which the most serious are constipation and possibly ileus, depend on the parasympathetic blockade. Application requires considerable skill on the part of the physician, and the agent should be reserved for cases of grave hypertension.

The powerfully acting diuretic, chlorothiazide, has also been applied in hypertension. If it is given as a supplement to a ganglion-blocking agent, there is often increased fall in blood pressure, especially orthostatic; the dose of the ganglion-blocking agent can, as a rule, be reduced. In patients with edemas, either as a complication in the ganglion-blocking treatment or because of heart insufficiency, chlorothiazide usually has a brilliant effect. Preliminary experiences in Bispebjerg Hospital with chlorothiazide applied with ganglion-blocking agents show that it means a great advance in the treatment of patients with edemas, but it is necessary to guard against hypokalemia during the treatment. Veratrum alkaloids give reduced blood pressure by stimulation of the afferent part of the reflexes decreasing blood pressure and by central effect. With careful adjustment of the dose, a marked fall in blood pressure without side-effects results in some cases.

Medicamental treatment of hypertension should be applied in malignant hypertension and in premalignant hypertension, in marked hypertension and heart insufficiency, and in repeated cases of acute hypertensive encephalopathy. More relative indications include cases of hypertension and angina pectoris, headache on a hypertensive basis which is not improved by other treatment, and cases with a continuous diastolic pressure of 135 mm. Hg or more. At present the greatest difficulties as to the indication for medicamental treatment are presented in the group of patients with labile hypertension with no or slight organic changes. Often indications for treatment and the method will be modified by special conditions.

Dithiazanine, a New Vermifugal Polyvalent Agent with Activity Against Strongyloides, Trichuris and Oxyuris. L.-C. Brumpt and Ho-Thi-Sang. Presse méd. 67:289-290 (Feb. 14) 1959 (In French) [Paris].

Dithiazanine is a polyvalent vermifugal agent which in the form of sugar-coated tablets was given a therapeutic trial in 21 patients who were carriers of various species of nematodes. Of the 21 patients, 5 were carriers of Oxyuris organisms, 6 were carriers of Strongyloides stercoralis, and 14 were carriers of Trichuris parasites. The drug was given in doses of 40 mg. per kilogram of body weight 2 or 3 times daily, with a maximum daily dose of 600 mg. for adult patients. Neither fasting nor purging was required. The drug in the doses used proved to be not toxic; it was not absorbed by the alimentary tract but was excreted in the feces, the color of which turned blue. The duration of treatment varied, depending on the type of the intestinal parasites and the degree of infestation.

Dithiazanine showed a pronounced activity against S. stercoralis, being superior in this respect to all other anthelmintics known to the authors. Administration of 600 mg. daily for 21 days resulted in a complete cure in 3 of the 6 patients. Short and repeated courses appeared to be less effective. Follow-up studies should be made with the aid of cultures of feces and duodenal tubage for several months. The drug also proved to be highly active against trichuris parasites. A 5-day course of treatment was required for patients with mild infestation, and a course of at least 10 days for those with severer infestations. Follow-up studies by direct counts of eggs in the feces and enrichment techniques should be carried out for at least 3 weeks after the termination of the treatment. Dithiazanine showed the same activity as piperazine against Oxyuris organisms. A 5-day course with daily doses of 300 to 500 mg. proved satisfactory but should be repeated. Follow-up studies, with the aid of the adhesive Cellophane technique, should be carried out every week for one month.

Dithiazanine was also given a trial in 15 patients with ascariasis but proved to be inferior to piperazine and even inferior to santonin and Chenopodium. It was ineffective in 10 patients with ancylostomiasis.

PATHOLOGY

Cancer of the Common Bile Duct. J. Benhamou, A. Gottfried, F. Darnis and R. Fauvert. Semaine hôp. Paris 35:89-100 (Jan. 12) 1959 (In French) [Paris].

The authors draw conclusions about cancer of the common bile duct (excluding the hepatopancreatic ampulla) from observations of 17 cases during 1947-1957 in 3 medical services of the Public Assistance of Paris. The presence of this type of cancer was noted in 1% of autopsies and was the cause of 1% of all icterus cases and 0.058% of the admissions to these medical services which specialize in hepatobiliary pathology. This disease affects principally persons 50 to 70 years old, with the same incidence for both sexes. Biliary lithiasis does not seem to have a part in the etiology. This is in contrast to cancer of the gall bladder where lithiasis is discovered in 60 to 80% of the cases. The appearance of cancer of the common bile duct is quite variable. In some cases it is in the form of a tumorous mass; in others, in the form of an induration of the walls of the duct. This polymorphism explains the errors sometimes committed in surgery and autopsy; a small cancer may be taken for a stone, a large cancer for an inflammatory induration. Cancer of the common bile duct may lie on any place along the duct, but it may have a selective localization at a bifurcation on a level with the porta hepatis. It can often extend along the main duct. In this series it extended along the intrahepatic biliary ducts ("fan-shaped" cancer) in 7 cases. Metastases of this cancer are frequent. The usual seats are the lymph nodes of the hepatic pedicle and the liver. In this series of 17, there were no metastases in 5 cases, but there were hepatic metastases in 7 cases and other metastases in 3.

Clinical symptomatology of cancer of the common bile duct is dominated by icterus. In 4 of the 17 patients icterus was the first sign of cancer; in 13 others there was a disturbed preicteric period marked by intense asthenia in 8 patients, loss of weight in 9, and anorexia in 10. Five patients had pain which was not intense in the epigastrium or right side of the hypochondrium. Enlargement of the liver was present in 15 cases, ascites in 4, and edema of the lower extremities in 4. Evolution of the disease is rapid. Death generally occurs 2 or 3 months after appearance of the first sign, and 1 or 2 months after the beginning of icterus in both patients who have been operated on and those who have not. This type of cancer, like cancer of the pancreas, gives the picture of obstructive icterus. It differs in that liver enlargement is greater, there is a relative absence of pain (which is frequent in cancer of the pancreas but was present in just 25% of this series), there is a relative absence of enlarged gallbladder (10% of the series), and the disease progresses very rapidly.

In this series functional hepatic investigation showed a retention syndrome and negative flocculation tests. In some patients with obstructive jaundice there were unexpected observations: the increase in bile salts was less than would have been suggested by the presence of bile pigments in the blood, and there was a fall in the level of esterified cholesterol. The usual anemia and hyperleukocytosis were present. The authors did not perform transhepatic cholangiography, but believe that it allows diagnosis of cancer of the hepatic duct bifurcation. This examination shows large dilation of the intrahepatic biliary ducts and complete blockage at the level of the hilus of the liver. These complete hilar blockages are almost always of the nature of a neoplasm, which, in turn, is almost always cancer of the biliary ducts. Laparoscopy is useful in the etiological diagnosis of icterus. In one case of cancer of the hilus, which is the most frequent localization of cancer of the common bile duct, a large green liver due to cholestasis and a normal or flaccid gallbladder were noted. The only treatment for cancer of the common bile duct is surgical. In this series surgery generally had mediocre results.

Endocrine Function of a Heterotransplantable Human Embryonal Carcinoma. G. B. Pierce, F. J. Dixon Jr. and E. Verney. A. M. A. Arch. Path. 67: 204-210 (Feb.) 1959 [Chicago].

The authors recently reported on Pitt 61, an embryonal carcinoma of the human testis heterotransplanted to cortisone-treated hamsters. Some of the animals with grafts of Pitt 61 had an associated uterine hyperplasia, and their tumors required 30% less time to attain transplantable size than those associated with small uteri. At that time, neither the hormone responsible for the large uteri nor the role of the tumor in the production of the hormone had been identified. The experiments recorded in this paper indicate that Pitt 61 produces chorionic gonadotropin in amounts capable of causing significant uterine hyperplasia in approximately 20% of hosts grafted with the tumor. The majority of students of testicular tumors have taken the stand that, when an embryonal carcinoma was found in a patient with elevated serum chorionic gonadotropin, elements of choriocarcinoma were most likely hidden either in the primary tumor or in a metastasis.

By serial passage of the tumor over the past 3 years, the authors were able to examine more than 3,000 microscopic sections prepared from some 1,500 grafts of Pitt 61, and they never found areas of choriocarcinoma. As a result they conclude that Pitt 61 is an embryonal carcinoma sometimes capable of secreting chorionic gonadotropin. The presence of an embryonal carcinoma with the function of trophoblast strongly supports the contention of Friedman and Moore and Dixon and Moore that embryonal carcinoma is a stage in the morphogenesis of choriocarcinoma. Hormone-secreting tumors grew significantly faster than nonhormone secretors. The growth rate of Pitt 61 was stimulated by the administration of chorionic gonadotropin to the heterologous hosts but not by the administration of follicle-stimulating hormone.

Unrecognized Myocardial Infarction: A Clinicopathologic Study. W. J. Johnson, R. W. P. Achor, H. B. Burchell and J. E. Edwards. A. M. A. Arch. Int. Med. 103:253-261 (Feb.) 1959 [Chicago].

Myocardial infarcts, especially healed ones, are often discovered at autopsy when they had not been recognized clinically. In order to ascertain the incidence of clinically unrecognized myocardial infarctions, the authors selected 143 patients, with either acute or healed myocardial infarction or both, for study out of a total of 1,267 autopsies performed at the Mayo Clinic during the years 1953-1954. In 57 of 113 patients with healed infarcts, the condition had been clinically diagnosed or suspected. In 56 patients there was no clinical diagnosis or recorded suspicion of previous myocardial infarction. Of 63 patients who died during acute myocardial infarction, 38 had a correct clinical diagnosis and 25 did not. The most important factor in the failure to recognize healed or acute infarcts was the absence of angina pectoris or of a history of prolonged thoracic pain. Such a history was obtained almost twice as frequently in patients with healed infarcts who were seen repeatedly as in patients who were seen only for their terminal illness. However, even among the patients who were seen repeatedly, there was an appreciable number (41%) who had no history of angina pectoris or of previous acute substernal pain, even though severe coronary atherosclerosis and gross myocardial scars were present at autopsy.

The coexistence of acute dyspnea, congestive heart failure, hypertension, or diabetes mellitus did not appear to influence greatly the incidence of correct antemortem diagnosis. The average age of patients with undiagnosed acute infarction was 4 years greater than that of patients with recognized infarction, but the sex distribution was the same in the 2 groups. Correct antemortem recognition was somewhat more frequent when the lesions were conglomerate and transmural in extent rather than patchy and subendocardial. Among the transmural infarcts those located laterally were more often unrecognized, while among the subendocardial infarcts those situated laterally and posteriorly were more difficult to diagnose. These differences in frequency of recognition were unrelated to the incidence of pain and were probably related to the increased likelihood of obtaining electrocardiographic confirmation when myocardial infarction occurs anteriorly.

The electrocardiogram gave supportive evidence of myocardial infarction in 29 of 47 patients in whom electrocardiographic examination was performed after the estimated onset of the infarction. It is suggested that these results probably reflect an insufficient number of follow-up electrocardiograms in patients whose symptoms did not strongly suggest myocardial infarction and are not a good index of the diagnostic accuracy of the electrocardiogram. A history of characteristic thoracic pain was often absent when infarction occurred in the immediate postoperative period, was accompanied by shock, occurred in patients who had concomitant strokes or sudden occlusion of other major arteries, and occurred in those whose state of consciousness was altered by other systemic diseases.

Absence of Intercapillary Glomerulosclerosis in the Diabetic Patient with Hemochromatosis. P. Lonergan and S. L. Robbins. New England J. Med. 260:367-370 (Feb. 19) 1959 [Boston].

The authors reviewed the clinical records and postmortem microscopic renal sections of 62 patients with so-called diabetes incident to hemochromatosis. The proportion of male to female patients was 14 to 1. Most of the patients were 50 to 70 years old. The diagnosis of hemochromatosis was established in each case at autopsy, and the existence of diabetes was established by review of the clinical records. In 21 of the 62 patients the onset of diabetes occurred 5 to 19 years before death. No lesions of intercapillary glomerulosclerosis were found in any of the 62 patients with hemochromatosis, including the 21 patients having diabetes for 5 years or longer. The absence of intercapillary lesions in this small series represents a statistically valid difference from a comparable group of patients with diabetes mellitus.

The authors suggest on the basis of this study that Kimmelstiel-Wilson lesions probably do not occur in the patient with so-called diabetes incident to hemochromatosis. Two interpretations of these results are given: 1. The factor responsible for the carbohydrate changes cannot also be directly productive of the renal lesions of Kimmelstiel-Wilson disease. Thus, it is suggested that diabetes mellitus is a complex disorder having aberrations in carbohydrate metabolism and a propensity for vascular disease, the two being closely related but not mutually interdependent features. 2. The so-called diabetic state in hemochromatosis differs significantly from diabetes mellitus; the two at least are unlike as regards the occurrence of intercapillary glomerulosclerosis. It is proposed that the diabetes associated with hemochromatosis be referred to only as insulin deficiency or hyperglycemia rather than by the term "diabetes mellitus."

Other authors have commented on the lack of predisposition to atherosclerosis in patients with hemochromatosis. The absence of renal glomerular lesions in the patients of this series adds further weight to this view and underscores the importance of differentiating the various disorders that have in common only the defective utilization of carbohydrate. These findings further support the thesis that the derangements leading to vascular lesions in the patient with diabetes mellitus are not necessarily directly related to the defect in carbohydrate utilization. Many of these areas will require study before it can be conclusively stated that indeed the diabetes of hemochromatosis is not diabetes mellitus.

Fibrosis of the Breast. P. S. Vassar and C. F. A. Culling. A. M. A. Arch. Path. 67:128-133 (Feb.) 1959 [Chicago].

Of 500 biopsy specimens of breast tissue examined annually in the department of pathology of the Vancouver General Hospital, about half prove to be benign lobular hyperplasia. It is generally accepted that lobular hyperplasia is a mammary dysplasia affecting stroma as well as epithelial elements. One uncommon variant consists of a pure stromal lesion, the fundamental picture of which consists of a dense and amorphous deposition of collagen within the mammary stroma. This variant has been referred to as "fibromatosis," "fibrosis of the breast," or "fibrous disease of the breast." The authors collected from their files the records of 20 patients with this lesion, whose ages ranged from 17 to 49 years. The lesion presented as a palpable mass, usually well localized and occasionally slightly tender. It most frequently was located in the upper outer quadrant of the breast. On palpation the lump was of moderate firmness, so that it could be mistaken for carcinoma. It was almost never more than 5 cm. in diameter, but in 2 patients simple mastectomy was performed for widespread involvement of the breast parenchyma. While the authors did not attempt a detailed investigation of possible associated hormonal imbalance, they gained the impression that a number of the patients had a history of menstrual irregularity and sterility.

With the use of the standard hematoxylin-and-eosin staining techniques, the authors examined multiple sections of breast tissue specimens of the 20 patients with fibrosis and of 5 representative cases of mazoplasia, 50 normal autopsy specimens in different age groups, and 200 specimens of benign cystic disease. They believe that fibrosis of the breast represents a form of benign lobular hyperplasia and has a similar origin in hormonal imbalance, probably hyperestrogenism. Chemical and histochemical analyses of these lesions revealed them to be composed of apparently normal collagen, although of a rather sclerotic nature, similar to that seen in prolonged hyperestrogenism or aging. Discussing the morphogenesis, the authors suggest that focal mazoplasia possibly precedes the fibrosis. The sequence of events is believed to be initiated by excessive and prolonged intralobular ground substance deposition, with subsequent transformation into collagenous tissue.

Haemolysis Caused by Tubing in Extracorporeal Circulation. J. W. Stewart and M. F. Sturridge. Lancet 1:340-342 (Feb. 14) 1959 [London].

Hemolysis in a pump-oxygenator circuit, designed for experiments on extracorporeal circulation in dogs, prompted the authors to investigate the effect of the tubing on the blood. Samples of new tubing made from red rubber, translucent rubber, siliconed rubber, crystal-grade polyvinyl chloride, polyvinyl chloride, and beverage hose, having the same internal diameter (6 mm.), were cut into equal lengths (45 cm.). Each tube was partly filled with heparinized blood, which was freshly drawn from the same human donor. The ends of each tube were joined, thus forming a closed circuit in each tube. The circuits were then placed on a vertical disk and turned in their long axes at 17.5 rpm for an hour. By this method a continuous flow at constant velocity was produced through the circuits by gravity, and the effects of using a pump were avoided. The velocity of flow was 7.8 m. per minute, which is equivalent to a flow rate of 222.5 ml. per minute. At the end of an hour the blood in each circuit was analyzed for plasma hemoglobin. In later experiments one additional type of tubing was tested, Tygon (S-22-1). As a control, the same quantity of heparinized blood (3 ml.) was left standing in a 3-by-0.5-in. glass tube. This experiment showed hemolysis of different degree in the circuits.

The experimental conditions were thought to be more severe than would be met during extracorporeal circulation of the same duration, since all the blood was circulating continuously and had no respite in reservoirs or in the body. It was found that blood flowing through tubing was destroyed to an extent which varied with the material from which the tubing was made. Washing the tubing through before use did not materially alter this effect. Storage of heparinized blood before use appeared to increase the liability to destruction. Temperature, within the range tested, i. e., from 20 to 37 C (68 to 98.6 F), had no effect. For any given tube, there appeared to be a critical velocity of flow, which, if exceeded, produced hemolysis. High rates of flow can be obtained with tubing of wide internal diameter and low destructibility. Dilution of the blood with physiological solutions decreased the liability to destruction. In general, the smoother the internal wall of the tube, the less hemolysis was produced.

The conclusion from these experiments is that, of the materials tested, only beverage hose and Tygon (S-22-1) tubing are suitable for use in a pump-oxygenator at the rates of flow desired. The recommended internal diameters of these tubes are: 6 mm. for flow rates up to 110 ml. per minute; 12 mm. for flow rates up to 900 ml. per minute; 24 mm. for flow rates up to 7 liters per minute. Within the limits of extracorporeal circulation, these diameters allow flow without hemolysis indefinitely.

Toxoplasmosis: A Dye-Test Survey on Sera from Vegetarians and Meat Eaters in Bombay. B. D. Rawal. Tr. Roy. Soc. Trop. Med. & Hyg. 53:61-63 (Jan.) 1959 [London].

The author points out that Garnham in 1957 had suggested that the high incidence in man of positive reactions in the dye test for toxoplasmosis might be due to eating meat containing Sarcocystis organisms, and he suggested immunization against toxoplasmosis by means of such organisms killed by cooking. Rawal considers it more likely that the high incidence of positive reactions to toxoplasmosis is due to eating meat containing Toxoplasma organisms, dead or alive, for there is no evidence that in man Sarcocystis infection gives rise to antibodies giving positive reactions in the dye test for toxoplasmosis. In either case it should be possible, as Garnham said, to clear up the point by examining serums from vegetarians and meat eaters. It was possible to do this in Bombay where vegetarians and meat eaters live in the same area under similar conditions and eat the same food with the exception of meat. Both consume vegetables, cereals, and fruits and also boiled milk and products made from boiled milk. The vegetarians do not eat eggs, but the meat eaters do so. Meat is usually submitted to 2 hours' boiling in salt water before it is spiced and eaten.

Serums were obtained from 246 Christians and Moslems who ate meat and from 141 Hindus who did not. The serums were refrigerated until they were examined in Sheffield by the dye test of Sabin and Feldman, as standardized by Beverley and Beattie. At the same time serums from 224 healthy adults in the Sheffield area were tested. At a titer of 1:16 the percentages of positive results were for Bombay meat eaters, 18%, for Bombay vegetarians, 21%, and for Sheffield adults, 14%. The consumption of cooked meat (mainly mutton and chicken) in Bombay has no effect on the incidence of Toxoplasma antibodies. It seems unlikely that beef and pork have an important influence, for the incidence of antibodies is nearly the same in Sheffield and Bombay.

RADIOLOGY

The Accuracy of Radiology in Demonstrating Ruptured Intracranial Aneurysms. L. V. Perrett and J. W. D. Bull. Brit. J. Radiol. 32:85-92 (Feb.) 1959 [London].

In an attempt to assess the accuracy of the angiographic demonstration of intracranial aneurysms causing spontaneous subarachnoid hemorrhage, an analysis was made of 210 patients with subarachnoid hemorrhage, all of whom had a ruptured aneurysm and submitted to cerebral angiography, and in each of whom the diagnosis was confirmed at autopsy. Of the 210 patients, 187 had their aneurysms accurately shown radiologically, i. e., the angiographic accuracy was 89%. The causes of erroneous radiologic diagnosis were studied in the remaining 23 patients who were subdivided into 5 groups. In 5 of the 23 patients, spasm that prevented filling of the aneurysm by the contrast medium was responsible for the diagnostic error; in 6 patients, the examining radiologist misinterpreted the visible aneurysm as a vessel loop (observer's error); in 4 patients, inadequate examination, because of a paucity of projections taken at different angles, caused the diagnostic failure; in 4 patients, the smallness of the aneurysm was responsible for the normal appearance of the arteriograms even in retrospect after the most careful scrutiny; in the remaining 4 patients who had more than one aneurysm, an intact aneurysm was observed, but a second aneurysm (ruptured) was not observed. In none of the patients did thrombosis prevent the angiographic demonstration of an aneurysm, and it is felt that thrombosis has been blamed too readily in the past for discrepancies in radiologic and autopsy findings. The value of projections, such as the perorbital view, in addition to routine anteroposterior, lateral, and oblique views, is stressed. The authors believe that the potential accuracy of radiologic diagnosis of cerebral aneurysm is about 96%.

Anomalous Development Induced in the Embryonic Rat by the Maternal Administration of Radiophosphorus. M. R. Sikov and T. R. Noonan. Am. J. Anat. 103:137-161 (July) 1958 [Philadelphia].

The authors felt that in view of the increasing use of radioactive materials more information is needed about the effects of maternally administered radioactive materials on embryonic and fetal development. The effects of maternal roentgen-ray irradiation having been established by other investigators in terms of the growth and development of the rodent fetus, the authors of this report decided to investigate the results of the more prolonged beta-radiation of maternally administered radiophosphorus (P^{32}). Female rats of the Wistar albino strain which had been bred to males of the same strain were injected intraperitoneally after 6, 8, 9, or 10 days of gestation with a dose of between 0.3 and 2.0 mc. of P^{32} of high specific activity, made up in isotonic sodium chloride solution. Test and contratest animals (the latter having been injected only with isotonic sodium chloride solution) were killed at intervals for determination of radioactivity and for study of the progressive changes occurring after irradiation. The uterus was immediately excised, and all the embryos and fetuses were weighed, measured, and examined for gross malformations. Randomly selected fetuses from each litter after suitable preparation were serially sectioned, stained, and examined.

It was found that the incidence of gross malformations of the face, limbs, and eyes increased with increasing dose after injection of P^{32} on the 6th day and to an indefinite extent on the 8th day of gestation. Correlations between the incidence of anomalous growth and administered dose were not readily apparent after injection on the 9th or 10th day of gestation. From measurements of P^{32} concentrations in fetal and adjacent maternal tissues at various times after injection of the radioactive material, it was possible to calculate the amount of radiation, expressed as roentgens equivalent physical (rep), received by the fetus during any interval. When the results of these experiments were compared with those found after acute roentgen-ray irradiation, it was found that the amount of radiation required to produce a comparable incidence of malformations of the face seems to be higher with P^{32} than with roentgen-ray irradiation. The most striking difference between the results obtained by these authors with P^{32} and those of investigators employing a single exposure to external roentgen-ray irradiation was in the effects which followed the administration of P^{32} on the 6th or 8th day of gestation. The ability of P^{32} to produce malformations when injected at a period in gestation during which a teratogenic effect of roentgen-ray irradiation has not been demonstrated is not easily explained.

It is tempting to ascribe these effects to the persistence of radiation due to the P^{32} injected on days 6 or 8 into the period during which roentgen-ray irradiation produces malformations. While this possibility cannot be completely excluded, the authors feel that it is not sufficient to explain the results, and that no single factor can be designated as being responsible for the difference between these 2 types of irradiation.

Different Behavior of the Extrahepatic Bile Ducts Under the Influence of Morphine: Cholecystocholangiographic Research. G. C. Masini. Nuntius radiol. 24:809-833 (Nov.) 1958 (In Italian) [Florence, Italy].

Routine cholecystocholangiographic examination revealed no abnormalities in 8 patients suspected of cholecystopathy. Different results were obtained on a subsequent examination in which the patients were first given a subcutaneous injection of 1 cg. of morphine. Fifteen minutes after the administration of morphine they were given an intravenous injection of 30 cc. of Biligrafin. Four roentgenograms were then taken, one every 15 minutes; a 5th roentgenogram was taken after 2 hours. Additional roentgenograms were taken after the patients had been given a fat meal. The gallbladder 2 hours after the administration of the contrast medium became larger in volume than it usually did when morphine had not been given and appeared more homogeneously opaque. The extracholecystic bile ducts remained opaque for a period longer than usual. Results after the intake of the fat meal changed from case to case. The administration of morphine caused painful symptoms in all the patients. The author believes that in patients with gallbladder disease this opium alkaloid has a spastic effect on the choledochoduodenal sphincter and a depressive effect on the tone and on the contractility of the bladder. This effect seems to be conditioned by some preexisting factor, present in the extrahepatic bile ducts, strictly related to the neurovegetative orientation of the patient. Morphine can be used in gallbladder tests: in normal cases it may be used to test the tone and the contractility of the gallbladder; in patients with suspected gallbladder disease it may reveal particular dystonic states of the extrahepatic bile ducts.

BOOK REVIEWS

Physical Diagnosis: The History and Examination of the Patient. By John A. Prior, M.D., *Professor of Medicine, Ohio State University College of Medicine, Columbus*, Jack S. Silberstein, M.D., *Clinical Associate Professor of Medicine, Ohio State University College of Medicine*, and contributors. Cloth. $7.50. Pp. 388, with 193 illustrations. C. V. Mosby Company, 3207 Washington Blvd., St. Louis 3, 1959.

This book teaches in an orderly, concise manner how to take a good history and do a complete physical examination. Contributors are from the faculty of Ohio State University, and the book is well edited to give proper balance to each area. Each region of the body is treated in a simple and yet surprisingly complete manner. The book is not cluttered with unnecessary detail. It is well illustrated and the explanatory diagrams are excellent. In a relatively short space the chapter on the history of the patient covers the pertinent information sought. Due to the frequency and the importance of functional disorders there could have been more emphasis in this portion of the book on determining the emotional maturity and stability of the patient. By necessity, the book is strongly oriented toward the organic, but in history-taking the student also should be prompted to watch the patient's emotional relationships to those closest to him, emotional and illness reaction patterns during each crisis, and emotional stresses at the time of onset of each illness, and finally to correlate these with the behavior of the patient during the more unpleasant parts of the examination.

Not much space is devoted to specific diseases, but emphasis is properly placed on how to obtain significant information and positive findings. Enough common disease entities and pathological conditions are mentioned to be informative, to give meaning to the methods used, and to stimulate interest. Although written primarily to teach the medical student, the book is so thorough and practical that every doctor doing physical examinations could profit by reading it. The general practitioner should find the eye, ear, nose, and throat chapters especially useful. For example, laryngoscopy, which is not performed as often as it should be, is simplified and explained well in a few pages. Also, the neurological section, especially where it deals with study of the cranial nerves and the spinal cord, provides a good review of this portion of the physical examination which is sometimes not made as thoroughly in office practice as the clinical condition may indicate. The final chapter on pediatric examination presents a helpful résumé of the additional procedures needed for studying infants or children.

In the next edition a chapter might be added on the annual physical examinations of presumably healthy persons and the industrial physical examinations of those who pretend to be well and fit to work. This could provide information on obtaining the work records and histories of emotional problems causing job changes, illness, or absenteeism. Explanations of tests to record accurately the near vision, color perception, hearing, and vital capacity might be included. Present day otometers and spirometers provide other accurate and helpful records. The groins of women, especially in preemployment physical examinations, must be routinely examined in the upright position or hernia will be missed. The authors have taken a large subject and presented the essentials in an interesting, well-balanced, and commendable book.

Diseases of the Colon and Anorectum. Volumes One and Two. Edited by Robert Turell, M.D., *Associate Surgeon and Chief, Rectal Clinic, Mount Sinai and Montefiore hospitals, New York City.* Cloth. $35 per set. Pp. 608; 609-1238, with 634 illustrations. W. B. Saunders Company, 218 W. Washington Sq., Philadelphia 5; 7 Grape St., Shaftesbury Ave., London, W. C. 2, England, 1959.

Within these two volumes Dr. Turell, aided by 82 distinguished contributors, has collected precise, comprehensive, and authoritative information about the colon and anorectum, and thus created a practical, progressive, and complete textbook on this subject. He has achieved the goal of presenting newer concepts as well as established principles.

Approximately three-fourths of the subject matter concerns rectocolonic and anorectal lesions; the rest covers applied basic science, diagnosis, and anesthesia. The scope of the basic material ranges through the embryology of the alimentary tract; the anatomy and physiology of the colon; endocrine factors during and after major surgery; water and electrolyte imbalance; nutritional, pharmacological, and bacteriological factors as related to the colon; and chemotherapeutic agents applied to surgery of the colon. These chapters are clear, comprehensive, and well documented. Snyder's section on embryology is complete, and his three-dimensional diagrams are most instructive. The section on anatomy by Goligher of St. Mark's Hospital for Diseases of the Rectum and Colon, London, cites much of his basic work and corrects several time-honored misconceptions. The chapter on fundamentals of body fluid and electrolyte imbalances is

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brief in spots, but further information is incorporated in the succeeding article by Roberts which covers basic material in electrolyte abnormalities.

The diagnosis of anorectocolonic diseases and the anesthesia available for surgical correction of such lesions are well covered. In the former section an extensive description of the examination of the patient, including endoscopy of the colon and anorectum from the experience of Turell, is particularly good. The long chapter on roentgenologic aspects by Paul and Juhl of the University of Wisconsin is most comprehensive. Next appears Stout's illuminating treatise on benign tumors of the colon and rectum exclusive of adenomas. The latter are the subject of a separate chapter by Turell and Brodman, which includes detailed descriptions of endoscopic and open operative procedures designed to remove these common lesions. Concerning the potential malignancy of adenomas the authors present the evidence on both sides of the question and venture the opinion "that colorectal adenomas in some individuals have a propensity to undergo malignant transformation, while adenomas in other persons may remain benign." However, they advise extirpation of all rectocolonic adenomas on recognition, in the absence of systemic contraindications, even if only a minority of such adenomas become cancers.

Cancer of the colon in all its aspects is extensively covered. The article by DePeyster and Gilchrist on the pathology and manifestations of this disease is excellent, and the chapter by Southwick and Cole concerning prophylactic and adjuvant measures used during operation and postoperatively in the treatment of patients with carcinoma is most significant. Much original laboratory work is cited to emphasize the spread of cancer during operations, such as along the lumen of the intestine, within the peritoneum, through the lymphatics, and by way of the blood stream. The use of anticancer chemical compounds to combat these extensions is well documented. This is the best of current thinking on how to save more lives of patients with cancer of the intestine and other areas.

Considerable space is given to the choice and technique of operations for cancer of the colon, the various procedures being broadly described and well illustrated. The ascending colon has a lower rate of carcinoma than the descending, but it still is a most important area requiring fundamental knowledge of anatomy and of the local spread of cancer in order to carry out a well-planned operation. More space could have been devoted to it. Chapters on radon seed implantation and radiotherapy conclude the section on cancer of the colon and close the first volume.

The second book begins with excellent sections on intestinal obstruction, volvulus, and diverticulitis, the latter, by Rodkey and Welch, including many of the ideas expounded by the late Dr. Arthur Allen. The medical and surgical aspects of ulcerative colitis are well presented, and complications of both forms of therapy are evaluated quite fairly. This provides a fitting framework for the chapter in which Brooke presents the surgery currently employed in treating this disease. Finally, an ileostomy patient gives her ideas regarding postoperative rehabilitation, which should be of real value to many surgeons.

Lesions, diseases, and surgery of the anus receive appropriately extensive attention. Diagrams indicate the surgical techniques, and photographs illustrate many of the advanced pathological processes. Alternative surgical procedures are considered, and for all operations the important anatomic relationships are discussed. Miscellaneous subjects covered in the last portion of the second volume vary from developmental anomalies, teratomas, megacolon, and pilonidal disease to obstetric considerations in rectocolonic conditions. As would be expected office management is thoroughly described, since it is a large part of a proctologist's practice.

There is a tremendous amount of well-organized and excellently written material in these two volumes, since the editor has uniformly asked experts to write the various chapters. The work is recommended to every hospital and medical school library for ready reference by students, residents, and attending staffs. Those doing any colonic or anorectal surgery will find it a valuable source of general review and of more detailed information on specific problems. One does better surgery with such a wealth of knowledge at hand.

Breast Cancer: The Second Biennial Louisiana Cancer Conference, New Orleans, January 22-23, 1958. Edited by Albert Segaloff, M.D., Director of Endocrine Research, Alton Ochsner Medical Foundation, New Orleans. Sponsored by American Cancer Society, Louisiana Division, Inc. Cloth. $5. Pp. 257, with 43 illustrations. C. V. Mosby Company, 3207 Washington Blvd., St. Louis 3, 1958.

This report of the Second Biennial Louisiana Cancer Conference is truly a mine of up-to-date, succinctly presented information on all aspects of the problem of breast cancer. Its epidemiology is particularly well discussed by Day. The doubtful relationship of cancer to benign breast disease is emphasized, the increased incidence and drop in mortality is well defined, and the inverse relationship between breast and cervix cancer is established. Especially interesting is the discussion of familial incidence, with the lack of evidence for a milk factor. Epidemiologic studies of the type now under way by Wynder and Segi in Japan, where the disease is relatively rare, are clearly desirable.

McDonald's discussion of the biological variability of breast cancer should be read by every cancer worker, clinical or otherwise. He shows in beautifully documented form that 20% of patients have slowly growing benign disease, easily curable;

that 55% show remote metastases before the original disease is detectable; and that the prognosis is related to the time of treatment in only 25% of cases. This leaves the maximum curability rate at 45%, not too far from the actual figure or from that assumed by Haagensen if his criteria of operability are followed.

Attention is also called to the benign nature of sclerosing adenosis. The discussion of the care of terminal patients is a weak section. This is an important topic which needs attention. The discussion of the more extensive operative procedure described by Urban, for removal of the internal mammary chain of lymph nodes, is perhaps the most immediately significant part of the book. Of 290 patients 45% showed all nodes clear, but 36% had the internal mammary nodes involved. Of 25 patients with such involvement in whom the node chain was removed 8 were free of disease at the end of 5 years. If an increased salvage rate of 10% is to be expected from this procedure it should be routine, and no longer subject to debate.

The various presentations on roentgen therapy are of particular interest. They are somewhat like those which have been made for almost 60 years. It is concluded that the value of radiation in preoperative treatment is unproved, that it is the only useful tool in advanced, obviously inoperable disease if local deposits are to be discerned, and that the McWhirter procedure, simple mastectomy with irradiation of the axilla, is a remarkably effective procedure, presumably in McDonald's 45% of patients who tend to do well anyway. It is unfortunate that Escher did not document in greater detail his presentation of the effect of oncolytic agents in the treatment of breast disease refractory to other procedures. Further study of this topic is clearly in order.

The discussion by Segaloff of oophorectomy is rewarding, especially as it points out that the results are about as they have been (but not appreciated) for almost 50 years. The statement that "adrenalectomy adds nothing to oophorectomy" should be regarded with caution, even though it may be generally true. The general position that hormone therapy should precede operative interference warrants careful examination. The consideration presented of oophorectomy as prophylaxis against recurrence is exceedingly important and unfortunately inconclusive. A vigorous push in the area is clearly in order. The review of endocrine therapy is rewarding indeed, and encouraging. The undesirable side-effects of hormone treatment deserve the respect which they receive. The indications of better compounds to come are encouraging. Taylor's discussion of corticosteroid therapy is important, for both its practical and theoretical implications. The summary by Segaloff is excellent. This book is worth reading and rereading.

Neurological and Psychological Deficits of Asphyxia Neonatorum: With Consideration of Use of Primates for Experimental Investigations. By twenty-eight contributors. Edited by William F. Windle, Ph.D., Sc.D., Chief of Laboratory of Neuroanatomical Sciences, National Institute of Neurological Diseases and Blindness, National Institutes of Health, Bethesda, Md. Forewords by E. Harold Hinman, Ph.D., M.D., M.P.H., Dean of School of Medicine–School of Tropical Medicine, University of Puerto Rico, San Juan, and Pearce Bailey, Ph.D., M.D., Director of National Institute of Neurological Diseases and Blindness. National Institute of Neurological Diseases and Blindness symposia in neurology, William F. Windle, series editor. Cloth. $8. Pp. 336, with 83 illustrations. Charles C Thomas, Publisher, 301-327 E. Lawrence Ave., Springfield, Ill.; Blackwell Scientific Publications, Ltd., 24-25 Broad St., Oxford, England; Ryerson Press, 299 Queen St., W., Toronto 2B, Canada, 1958.

This monograph is the fourth of a series of published symposiums on neurology edited by Dr. Windle. It is a report of the transactions of a conference on asphyxia neonatorum, brain damage, and impairment of learning sponsored by the School of Medicine of the University of Puerto Rico and the National Institutes of Neurological Diseases and Blindness. A representative group of workers in this field participated in the conference and reported research on the various facets of the problem in progress in their laboratories and clinics. These presentations were interspersed with four roundtable discussions under the leaderships of Duncan Reid, Harold Himwich, John Churchill, and Willard Eyestone. The concluding remarks by Pearce Bailey are particularly significant and challenging.

Phelps made a conservative estimate that four children of every 1,000 births will develop manifestations of cerebral palsy. Thus, at least 16,000 new cases are added each year to our already large pool. Some 3% of our present population exhibits mental retardation when evaluated by the usual criteria. These figures present most convincingly the enormity of the problem and the importance of mobilizing all our research efforts to provide new knowledge to cope with it.

Several of the studies concerned themselves with the effects of asphyxia neonatorum and anoxia on behavior and structural changes in the nervous system of animals. The physiology of asphyxia neonatorum and the roles of hypothermia, endocrines, and the administration of oxygen were discussed. The relation of anoxia in early gestation to the production of teratologic defects was considered. The need for an ideal experimental animal for use in further research on the role of asphyxia, anoxia, and other factors in the production of mental retardation, cerebral palsy, and neurological complications was emphasized. The monkey is uniquely adaptable to psychological and sensory tests, and its reproductive process resembles that of man. The Cayo Santiago Primate Colony was described, and its possible increased use for studies on primates was explored. This monograph can be read with profit by research workers and clinicians interested in the physiology of oxygen supply and demand during pregnancy and in the many factors that interfere with its availability during critical periods in pregnancy, delivery, and the first few days of life.

Cellular and Humoral Aspects of the Hypersensitive States: A Symposium at the New York Academy of Medicine. Edited by H. Sherwood Lawrence, M.D., Associate Professor of Medicine, New York University College of Medicine, New York. Symposia of Section on Microbiology, New York Academy of Medicine, number 9. Cloth. $18. Pp. 667, with 120 illustrations. Paul B. Hoeber, Inc. (medical book department of Harper & Brothers), 49 E. 33rd St., New York 16, 1959.

The last decade or so has been a period of advance in our understanding of the processes concerned in allergy and in the broader aspects of hypersensitivity. This progress has largely been due to three factors. Special basic developments in technique, among which are the cellular transfer of hypersensitivity and fluorescing and isotopic labeling of antigens and antibodies, have permitted investigations along lines hitherto impossible, As a result of newer techniques and other considerations the concept of hypersensitivity has broadened in scope and interest to include autoimmunity, cancer, homotransplantation, viral and bacterial infection, and collagen diseases. The immunology of hypersensitivity has emerged from its ivory tower. Basic scientists in this field have become components of groups in which internists, physiologists, pharmacologists, enzyme chemists, surgeons, and others cooperate in the plans and aims of research.

This book contains 18 chapters on various basic aspects of hypersensitivity. Among the subjects covered are hypersensitivity to simple chemicals, the transfer of sensitivity of the delayed type, the biochemical factors involved in hypersensitivity responses, the immunology and pathogenesis of experimental and human serum sickness, agammaglobulinemia, the immunology of homologous tissue antigens, the whealing type of antigen-antibody reaction in man, experimental tissue injury induced by injections of emulsions of the same tissue; and cell changes in hypersensitivity reactions. The list of participants, collaborators, and discussants reads like a "Who's Who" in the field of hypersensitivity and includes such outstanding international authorities as Becker, Chase, Dammin, Dixon, Eisen, Freund, Gell, Heidelberger, Humphrey, Janeway, Kuhns, Lawrence, MacLeod, McMaster, Medawar, Monad, A. G. Osler, Pappenheimer, P. Y. Patterson, Stetson, L. Thomas, and B. Waksman. The organizational and editorial ability of H. S. Lawrence are amply reflected in the systemic coverage and the choice of contributors.

This volume crystallizes the personal experience of the participants as well as their immense knowledge of the field. It brings up to date under one cover material which would take years to glean from original papers and much of which is not yet published. The progressive internist, pediatrician, or surgeon should profit much from having this book on his shelf. For one who is interested in these mushrooming developments which affect a growing number of phases of medicine and for the *microbiologist, pathologist, immunologist,* and allergist this book is indispensable.

Vascular Surgery. By Geza de Takats, M.D., M.S., F.A.C.S., Clinical Professor of Surgery, University of Illinois College of Medicine, Chicago. Cloth. $17.50. Pp. 726, with 382 illustrations. W. B. Saunders Company, 218 W. Washington Sq., Philadelphia 5; 7 Grape St., Shaftesbury Ave., London, W. C. 2, England, 1959.

Although intended as such it is hardly a compliment to the author to call his book the finest written on the subject, since there has been a distinct lack of good books in this field. The present book, therefore, fills a real need. It covers the subject of peripheral vascular surgery but does not include cardiac or thoracic aortic surgery. The book is well organized and the writing is concise. The illustrations are numerous and well selected. The chapters on fundamental principles and diagnosis are superb. Of special interest is the inclusion in the appendix of simple illustrations of surgical incisions and operative procedures. In the preface the author states that the book is based on his personal experience. As a result undue emphasis is placed on sympathectomy as compared to reconstructive surgery. It is true, however, that sympathectomy is of fundamental importance and more useful than the enthusiasts of reconstructive surgery are prone to admit. It is questionable whether a chapter on essential hypertension needs to be included in such a book but, at least, in doing so, the author is contributing authoritative information.

Ulcerative Colitis: Treatment and Prognosis Studied on the Basis of 161 Cases. By John Lindenberg. [Thesis, M.D., University of Copenhagen. With Danish summary.] Translated from Danish by Elisabeth Aagesen. Paper. Pp. 118, with 14 illustrations. Christtreus Bogtrykkeri; [University of Copenhagen], Copenhagen, Denmark, 1958.

More than half of this small monograph is devoted to a systematic review of ulcerative colitis. In the series of 161 cases reported were 87 nonsurgical patients treated in Denmark during the years from 1929 to 1949. In the group treated surgically were 74 patients—18 treated at the surgical university clinic of the Rigshospitalet, Copenhagen, between 1952 and 1955; one elsewhere in Denmark; and 55 in America, some at the Massachusetts General Hospital, Boston, between 1941 and 1949, and others at the Edward J. Meyer Memorial Hospital, Buffalo, between 1941 and 1950. The basis for comparison of the American and Danish groups is admittedly small, since they were seen in different institutions at different times. The author concludes that the treatment of ulcerative colitis should be primarily medical; no specific effective therapy can be recommended on the basis of his findings.

Of the nonsurgical patients observed between 1929 and 1949 19% returned to full work capacity after prolonged treatment, and 30% died during an average observation period of 12 years. General clinical symptoms afford the best guide to therapy and prognosis. The review of previous contributions suggests that surgical treatment is indicated for regional ulcerative colitis; ulcerative colitis with particularly severe general symptoms; and ulcerative colitis with such complications as polyposis, colonic stricture, massive hemorrhage, impending perforation, fistula, certain cutaneous and ocular complications of a rheumatoid nature, arthritis, and incipient liver disease. The author suggests that operations such as subtotal colectomy and removal of the rectum have no effect or are contraindicated in patients with ascending ulcerative colitis. Ileostomy and subtotal colectomy performed in two stages are likely to cause fewer deaths than single-stage operations.

Diseases of the Nervous System Described for Practitioners and Students. By Sir Francis Walshe, M. D., D.Sc., F.R.S. With chapters on The Neurological Complications of Liver Disease, and Hepatolenticular Degeneration, by J. M. Walshe, M.R.C.P., Assistant Director of Research, Department of Experimental Medicine, Cambridge University, Cambridge, England. Ninth edition. Cloth. $8. Pp. 373, with 60 illustrations. Williams & Wilkins Company, 428 E. Preston St., Baltimore 2; E. & S. Livingstone, Ltd., 16 and 17 Teviot Place, Edinburgh 1, Scotland, 1958.

The appearance of a new edition of this textbook is evidence of its wide acceptance as an introduction to clinical neurology. The book includes well-written summaries of the major neurological disorders as well as abbreviated sections on the principles of neurological diagnosis. The chapter on vascular disorders of the brain has been enlarged to include a discussion of cerebral vascular insufficiency. The author mentions the use of anticoagulant therapy in the treatment of carotid and vertebral artery insufficiency, but he does not discuss the indications and contraindications. The chapter dealing with vitamin B_{12} deficiency has been expanded. A brief discussion of the brain stem —activating systems has also been added to this edition. The neurological manifestations of sarcoidosis and the collagen disorders, including polymyositis, are not described. The major deficit is the absence of references to aid the student or physican seeking detailed information on a neurological problem. The text is not sufficiently detailed to be of much use to the practitioner in need of a reference volume. The sections devoted to the treatment of neurological disorders include discussions of pharmacological agents and techniques which might be questioned by some authorities (e. g., the treatment of status epilepticus, the use of morphine in subarachnoid hemorrhage, and the use of vitamin E in muscular dystrophy). Despite these limitations the book contains many pearls derived from the great experience of an outstanding English neurologist.

Psychopharmacology Frontiers: Second International Congress of Psychiatry, Proceedings of the Psychopharmacology Symposium, [held in Zurich, Switzerland on September 2-4, 1957]. Edited by Nathan S. Kline, M.D., Director of Research, Rockland State Hospital, Orangeburg, New York. Cloth. $10. Pp. 533, with illustrations. Little, Brown & Company, 34 Beacon St., Boston 6; J. & A. Churchill, Ltd., 104 Gloucester Pl., Portman Sq., London, W. 1, England, 1959.

The publication of symposiums provides the interested reader with information which could not be obtained from a single author. This book contains the views of the world's leading authorities in the field of effective drug therapy in mental disease. The chapters are short, concise, and contain a minimum but necessary amount of statistical data. The large number of chapters results in a moderate amount of repetition, but this is an indication of general agreement. The progressive trend toward the pharmacological management of disturbed patients and away from the more traumatic methods used in the past should prove encouraging to the reader. The values of available drugs are described, as well as their limitations. An important contribution is the graphic description of the multitude of toxic reactions and side-effects that may occur with the clinical use of the phenothiazine and reserpine-like derivatives. Chapters on postulated modes of action of the drugs are included. An attempt is made to integrate the ascending reticular formation and hypothalamus with certain psychiatric disorders and their pharmacological treatment. The fact that serotonin metabolism plays an important role in integrative cerebral function is repeatedly emphasized. The suggested relationship between the mechanism of action of reserpine and serotonin in the central nervous system is especially interesting. The absence of an index makes this book difficult to use as a reference, but it should be useful to those interested in the current concepts of drug therapy in mental disease.

Surgery of the Stomach and Duodenum. By Claude E. Welch, M.D., D.Sc., Clinical Associate in Surgery, Harvard Medical School, Boston. Handbook of operative surgery. Third edition. Cloth. $9.75. Pp. 405, with illustrations by Muriel McLatchie Miller. Year Book Publishers, Inc., 200 E. Illinois St., Chicago 11, 1959.

This edition includes recent significant advances in the surgery of the stomach and duodenum. A brief discussion of some unusual diseases of the stomach amenable to surgical treatment has been added. As in previous editions the emphasis is on technique rather than discussion. The illustrations add much to the clarity of the text. The volume should prove particularly valuable to the young surgeon.

QUESTIONS AND ANSWERS

HYPERTHYROIDISM DURING PREGNANCY

To the Editor:—*What are the currently accepted theories and opinions regarding the indications and contraindications for the use of iodine and thiouracil to control symptoms of mild hyperthyroidism which have become more severe during pregnancy? Is there danger of the baby being a cretin if the mother receives no medication for her hyperthyroidism during her pregnancy? Will either drug itself cause cretinism in the fetus? Are laboratory tests of any value in determining the degree of hyperthyroidism during pregnancy?*

J. F. Doornbos, M.D., El Dorado, Kan.

Answer.—In the woman who has hyperthyroidism and who also is pregnant, the disease should be brought under control promptly because of the danger to both mother and fetus of continued hyperthyroidism. If the disease is mild, the administration of iodide solution may bring about an adequate remission. If the disease is more severe, control should be attained by the use of one of the antithyroid drugs, such as propylthiouracil. Lack of medication for hyperthyroidism during pregnancy probably will not cause the baby to become hypothyroid, but it does increase the risk of losing the fetus.

So far as is known, iodides will not cause hypothyroidism in the fetus, but in both human beings and experimental animals hypothyroidism has been observed in fetus when the mother has become hypothyroid during pregnancy while being treated with an antithyroid drug. Therefore, it is thought important that any woman treated for hyperthyroidism during pregnancy with an antithyroid drug should be given adequate replacement doses of desiccated thyroid as soon as she approaches the euthyroid state. A patient whose condition is maintained during pregnancy with adequate doses of antithyroid drug and desiccated thyroid should remain in a euthyroid state, and in these circumstances the baby should suffer no untoward results from either the hyperthyroidism or its treatment. The dosage of antithyroid drug required depends on the severity of the hyperthyroidism and the particular agent used. Of propylthiouracil, 150 to 200 mg. every eight hours usually is adequate for control of mild hyperthyroidism. A larger dose may be needed if the disease is more severe. As the euthyroid state is approached, the dose can sometimes be slowly decreased. The usual dosage of uncoated desiccated thyroid required in such patients is about 120 mg. per day.

Whether one elects to perform a thyroidectomy while the patient is pregnant or to wait until the termination of pregnancy before operating depends on many factors, including the stage of pregnancy when hyperthyroidism is discovered, the degree of hyperthyroidism, and the general condition of the patient. Usually in the middle trimester of pregnancy, with hyperthyroidism adequately controlled by the use of iodide solution or an antithyroid drug, thyroidectomy is tolerated without harm to mother or fetus. When the operation is performed earlier in pregnancy, the risk of fetal loss may be greater. If the patient is in the last trimester of pregnancy, it may be preferable to await normal parturition before proceeding with thyroidectomy. All of the usual laboratory tests for hyperthyroidism can be used in determining the degree of hyperthyroidism during pregnancy if the normal influence of pregnancy is taken into account. During pregnancy the basal metabolic rate and level of protein-bound iodine are elevated to moderate but not unusual degrees. Basal metabolic rates above +20% and protein-bound iodine levels about 12 mcg. per 100 ml. of serum are not ordinarily found in nonhyperthyroid pregnant women. Uptake of radioiodine by the maternal thyroid may be increased above normal during pregnancy, but tracer tests should not be made in pregnant women during any stage of pregnancy, even though it has been shown that the fetus does not collect radioiodine during the first trimester.

VAGINAL DISCHARGE IN CHILDREN

To the Editor:—*Aside from gonorrhea, foreign bodies, and pinworms, what are the causes of vaginal discharge in prepuberal girls? What should be done to discover the cause? What is the best treatment? Are estrogen creams or lactic acid douches of any value?*

Jack M. Troy, M.D., Hammond, Ind.

Answer.—Discovery of the cause of vaginal discharge in young girls is based on inspection for evidence of trauma or visible discharge, fresh and stained smears for pus cells, bacteria, Candida, and trichomonads, and vaginoscopic examination (not routine). Trichomonas and monilial vaginitis are the most frequent causes and should be treated as

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The answers here published have been prepared by competent authorities. They do not, however, represent the opinions of any medical or other organization unless specifically so stated in the reply. Anonymous communications cannot be answered. Every letter must contain the writer's name and address, but these will be omitted on request.

one would treat such infections in adults. Use of a sulfonamide vaginal jelly daily for one week may be prescribed if pus cells are present. If the discharge is due to Candida and if it persists, a gentian violet jelly in small applicators may be used. Should Trichomonas be present and resistant to the usual treatment, a clear jelly, containing chelating, wetting, and detergent agents, used locally is preferable to tablet insertion. While estrogens are frequently used in infants and young girls to alter the mucosa and increase resistance to various types of infection, they are not desirable for treatment of the preadolescent girl because of possible undesirable side-effects. This consultant would not recommend the use of douches for the treatment of discharge in young girls.

TREATMENT OF CARDIAC EMERGENCY

To the Editor:—*An apparently well, 65-year-old woman was operated on for a fracture of the hip. On her 15th postoperative day she was given 30 minutes of physiotherapy, including crutch-walking and parallel bar exercises. This was done in spite of an internist's diagnosis of mild coronary insufficiency. The next morning at 4:00 a. m. she awakened complaining of severe chest pain. She stated that she had never before had this type of pain and she was sure she was having a heart attack. The nurse gave her 60 mg. of codeine. There was no relief. At about 4:30 a. m., the nurse, without an order, gave her 0.6 mg. of glyceryl trinitrate. The patient had never been given this drug before. Her color, pulse rate, and general condition were good until 4:50 a. m. At this time she experienced a complete circulatory collapse. This occurred with alarming rapidity. An intern who saw her at 5:00 a. m. ordered 15 mg. of morphine sulfate, but the patient died at 5:30 a. m. This was a coroner's case, but no autopsy was performed. It seems that death was due to either coronary occlusion or pulmonary embolus. Is glyceryl trinitrate indicated in either of these conditions? If not, what reasons contraindicate it?*

L. C. Sutherland, M.D., Rushville, Ill.

Answer.—Glyceryl trinitrate, in adequate doses, causes relaxation of the coronary vessels. For this reason it is often used, probably with benefit, in the treatment of angina pectoris, in which the pain is thought to be caused by inadequacy of the coronary circulation. When, however, coronary occlusion produced by mechanical obstruction, such as an embolus or a thrombus, is present and is followed by myocardial infarction, it is questionable whether glyceryl trinitrate or any other vasodilator drug is of value. Indeed, some authorities believe that, since it also dilates other vessels and frequently produces a fall in blood pressure, it may even be harmful. Since the experts are in disagreement, some representative opinions from standard reference works are quoted here:

"Nitroglycerin is hazardous in the acute phase of acute myocardial infarction and should not be used. If the patient is first seen in his initial attack of cardiac pain, this drug should not be administered until the diagnosis of acute myocardial infarct has been excluded. In the presence of fresh coronary occlusion, administration of nitroglycerin may lead to a fall in blood pressure and precipitate massive infarction or death" (Textbook of Medicine, edited by R. L. Cecil and R. F. Loeb, ed. 9, Philadelphia, W. B. Saunders Company, 1955, p. 1335).

"It is possible that nitroglycerin sublingually, in small repeated doses, e. g., 0.2 mg. (1/300 gr.) every hour, or nitroglycerin ointment . . . may favor the development of collateral circulation and tend to limit the size of the infarct. Such doses do not cause significant decline in blood pressure, or any untoward symptoms in most patients. However, proof of the value of nitroglycerin as a drug for routine administration is lacking" (Principles of Internal Medicine, edited by T. R. Harrison and others, ed. 2, New York, McGraw-Hill Book Company, Inc., 1954, p. 1369).

"Nitroglycerin may also be employed as a diagnostic agent to differentiate between the pain of angina pectoris and that of acute coronary thrombosis. The pain of acute coronary thrombosis is not relieved by nitrate medication. Considerable caution is necessary because the patient with a fresh myocardial infarction may be in a state of collapse. . . . If pain persists, the existence of coronary occlusion is more likely. A second tablet may be given only after a suitable interval. The careless use of nitroglycerin in patients with acute myocardial infarction may cause dangerous ectopic tachycardia, collapse, and even death" (Goodman, L. S., and Gilman, A., Pharmacological Basis of Therapeutics, ed. 2, New York, the Macmillan Company, 1956, pp. 740-741).

In patients with pulmonary embolism there is little reason to expect favorable results from glyceryl trinitrate. The pulmonary vessels apparently do not respond to nitrites. Although no specific contraindication to the drug is known, this condition may be associated with severe cardiovascular disturbances and the hypotensive action of glyceryl trinitrate might easily prove harmful. The general management of such cases is ably discussed in a report to the Council on Pharmacy and Chemistry, "Current Status of Therapy in Coronary Artery Disease," by Ellis and Hancock (*J. A. M. A.* 163:445-450 [Feb. 9] 1957). One of the standard textbooks mentioned above may be consulted for current information on the management of pulmonary embolism.

LYMPHADENOPATHY IN CHILDREN

To the Editor:—*A school health physician, examining children on entering kindergarten or first grade with ages varying from 4½ to 7 years or slightly older, has noticed in a large percentage of them a prominent cervical adenopathy, varying from a small lentil-size to pea-size, in the anterior and posterior triangles, even extending near the occiput and at times including the submental region and axillary and inguinal areas. Examination of the scalp, throat, teeth, gums, and entire oral cavity reveals no overt lesions or abnormality. Leukocyte counts may vary from 6,000 to 11,000 per cubic millimeter, with normal hemoglobin level and, occasionally, about 5% eosinophils. These children have had no history of allergy or parasites. Roentgenograms of the chest may reveal at most some bronchial irritation which clears up subsequently. There are no subjective complaints other than an occasional history of spontaneous epistaxis with normal temperature. These children are active. What is the significance of the adenopathy? How does one rule out Hodgkin's disease and leukemia? Since these findings are so common, one hesitates to request a biopsy.*

M.D., New York.

Answer.—It is important, first of all, to know whether the local cervical or generalized lymphadenopathy is a recent development or whether it represents a chronic long-standing manifestation. If the adenopathy is generalized, infectious mononucleosis is the first diagnosis to be considered in young people and a careful qualitative study of the peripheral blood and a heterophil agglutination test should identify the disease in most such patients. A residual generalized lymphadenopathy often persists for months or years after what may have been a subacute attack of infectious mononucleosis. Only if the lymphadenopathy is recent should Hodgkin's disease be considered. Usually this is not a generalized manifestation early. The commonest location for the first appearance of Hodgkin's lymphadenopathy is the supraclavicular area of the neck, with the cervical chains next; the mediastinum is also frequently involved early. In Hodgkin's disease the lymphadenopathy becomes generalized late in the course. The best early diagnostic criteria are to be found in a careful study of the peripheral blood, where the red blood cells, hemoglobin level, and platelet count will be normal but the leukocyte count will be low normal or slightly leukopenic, with a moderate eosinophilia, a depression in the percentage of lymphocytes, and an increase in the monocytic elements. Given these blood findings and suggestive enlargement of the lymph nodes, a biopsy should be requested promptly, in order to confirm or disprove the diagnosis of early Hodgkin's disease.

Any of the acute or chronic leukemias should be diagnosed from a qualitative and quantitative study of the blood, and if there is any question after a careful study of the peripheral blood a bone marrow aspiration will almost certainly confirm any diagnosis of leukemia. It should never be necessary to recommend a lymph node biopsy to make the diagnosis of leukemia. If a newly observed lymphadenopathy in any part of the body persists beyond three months without showing evidence of regression, a lymph node biopsy should be urged in order to make certain that one of the progressive lymphomas is not present in an incipient stage.

SIDE-EFFECTS OF STEROID THERAPY

To the Editor:—*Could the so-called anti-inflammatory steroids cause peptic ulcers or only recurrence of a preexisting healed lesion? Do they reactivate healed corneal ulcers in patients with rheumatoid arthritis and others whose conditions have been maintained with steroids for a long time? Is there any relation between the amounts given and the occurrence of the unwanted side-effects? Is there any likelihood that, in some, the steroids, similar to pheochromocytoma, periodically are produced in sufficiently large amounts to cause the undesirable effects often obtained by oral administration?*

M. J. Tobias, M.D., New York.

Answer.—Although the clinical impression of many physicians has been that there is a cause and effect relationship between steroid therapy and peptic ulcer, there is as yet no conclusive statistical evidence that the anti-inflammatory steroids either cause peptic ulcer or are responsible for the activation of preexisting ulcers. In patients with rheumatoid arthritis, in whom this suggestion first occurred, so many ulcerogenic drugs are administered that it is difficult to evaluate the cause and effect relationship of steroids alone. Renewed attention to the natural incidence of peptic ulcer indicates that in such diseases as rheumatoid arthritis the frequency of peptic ulcer, in the absence of medication, may be 15 to 20%. In patients with ulcerative colitis who are given large doses of steroids, peptic ulcer is rarely observed. Several recent statistical studies indicate no increased incidence of peptic ulcer associated with steroid therapy, in spite of the clinical impression, but additional data seem desirable.

Ophthalmologists are becoming impressed with the increasing frequency of serious complications evolving from herpes simplex in patients given anti-inflammatory steroids, but there has been no statistical evaluation of the frequency of activation of corneal ulcers in patients given prolonged steroid therapy, compared with persons who have not received such treatment. Steroid medication in such patients probably should be withheld unless there is an unequivocal indication. Wide individual variation exists in the manifestations of side-effects and the dosage of steroids required to produce the untoward symptoms. For reasons not yet clear, some patients may tolerate large quantities of steroids with minimal side-effects, whereas others develop untoward manifestations, such as electrolyte imbalance, including hypokalemia, after relatively small doses.

In 1954 Thorne and co-workers reported an extended study of steroid excretion in one "cyclothymic" patient. This study indicated that in some way glucocorticoid excretion was depressed during the overactive psychic phase and returned to normal with return of the psyche to normal. This observation apparently has not been verified. Obvious defects arise in attempting general conclusions from the study of one patient. It is possible that variations in the secretion of specific steroids, values of which remain extremely difficult to determine and, therefore, are not ordinarily estimated, might coexist with fluctuations in the emotional state.

PROLONGED FEBRILE ILLNESS

To the Editor:—*A 20-year-old woman complains of back pain. At the age of 12 she had a febrile disease that came on suddenly. She did not have chills. She had a temperature of 101 to 102 F (38.3 to 38.9 C) for about six months. During this time she lost all of the hair on her head. She was not crippled. She had no external evidence of suppurative disease. The patient lived in a rural area, and blood cell counts were not made. She became emaciated and so weak that she could hardly move. After about six months, the fever gradually disappeared but the patient remained bedfast for many months and was weak for a total of two years. She then regained normal health and has been normally active since. Careful physical examination does not reveal anything of note. A roentgenogram of her chest is normal. What might this girl have had? Although she had been menstruating regularly for a little over a year at the onset of the illness, menstruation ceased during the illness and was never reestablished, even though she otherwise regained normal health. Why is this? One year ago she menstruated once, rather normally, after a large dose of estrogen, but menstruation immediately ceased again. Does she ovulate? Can she have children? Would further attempts at reestablishment of the menstrual cycle be indicated, and, if so, what medicament should be used?*

Duncan C. McKeever, M.D., Houston, Texas.

Answer.—Any answer to this question must be speculative. This patient's illness might have been typhoid. After such an infection, it would not be unusual for complete alopecia to occur nor would it be unusual for amenorrhea to occur, but, when normal health was restored, the menstrual periods should have returned also. It is possible, therefore, that the menstrual abnormality is not related to the original illness, unless the adenohypophyseal system was adversely affected by the long period of malnutrition. No mention is made of the pelvic status of this patient. This would have to be known in detail before an attempt at diagnosis could be made. Levels of 17-ketosteroid, follicle-stimulating hormone, and luteinizing hormone should be determined. If these are within the normal range, the cause of the amenorrhea must be sought elsewhere. It is important to know the size of the uterus and ovaries. Hypoplasia of the pelvic organs could cause the amenorrhea, and so could enlarged ovaries. Inasmuch as certain tests to determine ovulation, such as endometrial biopsy and cervical mucus studies, might be objectionable to a 20-year-old single girl, the physician could use transabdominal pneumoroentgenography. The films would differentiate between normal, smaller than normal, and larger than normal gonads and demonstrate uterine size and shape. Treatment would depend on the findings. A clue to whether ovulation occurs might be obtained from basal body temperature charts kept over a period of several months. The assumption is that, when a patient does not menstruate for long periods, she does not ovulate either. If the tests show no evidence of ovulation, naturally no conception would occur. It is important that the menstrual cycle be restored in a girl of this age, both for physical and psychological reasons. In the absence of ovarian pathology, cyclic therapy, with use of estrogen and progesterone, might be tried for several months and then withdrawn.

SPELLS OF UNCONSCIOUSNESS

To the Editor:—*A 70-year-old man has had a large hiatal hernia for an unknown length of time. A gastrointestinal series revealed the proximal half of the stomach to lie above the diaphragm. For the last few years he has had spells of losing consciousness, always at night. They are preceded by twitching. Usually there are copious gaseous eructations, and then the patient comes to. He has amnesia about these spells. When seen, he usually has already regained consciousness. His pulse rate is supposedly normal during these spells. Electrocardiograms and hematocrit levels have been normal. He had severe anemia prior to iron therapy. Physical examination after these spells has been essentially negative. Blood pressure readings have been normal. How could these spells be explained?*

Gideon Tropp, M.D., Elmira, N. Y.

Answer.—It is unfortunate that the patient could not be examined during the unconscious spell, since it is impossible to reconstruct events with certainty from the information at hand. As described, the spell does not fit any known symptom complex. A possible explanation is that the patient has a vagovagal reflex tripped off by distention of the intrathoracic portion of the stomach from a shaft of swallowed air or a shift of gastric contents and air from the subdiaphragmatic portion of the stomach to the part within the thorax. Vagovagal reflex syncope in a patient with a diverticulum of the esophagus was described many years ago by Weiss. A more remote possibility is that he might have a physiological disorder analogous to the dumping syndrome, associated with quick mechanical emptying of the portion of his entrapped stomach from above the diaphragm into the subdiaphragmatic portion. It is possible that he has a sensitive carotid sinus with a reflex fall in blood pressure or the direct central reflex in which neither blood pressure nor pulse rate falls on irritation of the carotid sinus to produce the syncopal attack. An observation of the patient during an attack with recording of the pulse rate and blood pressure and possibly an electrocardiogram might throw further light on these or other mechanisms.

THROMBOSIS OF RETINAL VESSEL

To the Editor:—*A 64-year-old man was fitted with glasses by an optometrist two months ago, providing 20/20 vision in his only eye, the other eye having been removed after an injury many years ago. About two weeks ago, he noted his vision to be failing and consulted the optometrist again, who found his vision much impaired and advised medical examination. On examination, no abnormality could be found except a sedimentation rate of 80 mm. in one hour (Westergren). Fundus examination by an ophthalmologist revealed thrombosis of one of the retinal vessels, with some retinal hemorrhages and exudate. The ophthalmologist was at a loss as to the cause and recommended some empirical therapeutic measures. The patient was hospitalized, and most of the usual laboratory tests were performed, including an L.E. cell test. All gave negative results except for the serum albumin-globulin ratio, which was 3:3.2 (early reversal). A roentgenogram of the chest was negative. History was negative except for coronary thrombosis three years ago. Please give suggestions as to the possible cause and advice about treatment.*

M.D., Connecticut.

Answer.—From the information given, one is justified in making a diagnosis of arteriosclerotic cardiovascular disease. If, however, the thrombotic vessel happened to be the superior temporal retinal vein (a rare occurrence), one should look for an occluded, pencil-hard temporal artery on that side. Temporal arteritis is commonly associated with blindness due to venous thrombosis, often followed later by secondary glaucoma. The eye should be tested every three months for glaucoma regardless of the type of thrombosis. If there is temporal arteritis, a section of the occluded artery should be removed surgically. The sedimentation rate of 80 mm. per hour confirms the diagnosis of cardiovascular disease. The early reversal of albumin-globulin ratio is not specific for retinal disease. The treatment of arteriosclerosis depends on one's belief in heparin, lipotropic drugs, vitamins, citrus extracts, rutin, iodides, and other agents. There are some eye drops which are said to improve the circulation of the retina, but their mode of action is obscure.

HEMATURIA AND ENDOCARDITIS

To the Editor:—*A 25-year-old man has had congenital heart disease, probably either a patent intraventricular septum or pulmonary stenosis associated with dextrocardia. Within the past two years he has had two episodes of subacute bacterial endocarditis caused by Staphylococcus aureus. Both times treatment has consisted of 10 million units of penicillin daily, given intravenously by slow drip, 1 Gm. of streptomycin daily, given intramuscularly, and 500 mg. of erythromycin given every six hours. Positive blood cultures have disappeared with this regimen, but with both attacks he developed gross hematuria, albuminuria, and some elevation of the nonprotein nitrogen level. Could the large amounts of aqueous penicillin possibly cause this renal complication, or is it due to the endocarditis?*

Robert W. Willett, M.D., Raleigh, N. C.

Answer.—Gross hematuria occurs during the course of subacute bacterial endocarditis. Before the successful use of antibiotics in this disease, observers noted its occurrence, more particularly, when blood cultures were negative. The pathological lesion was glomerulonephritis or renal infarction. Recurrent hematuria is also seen in the course of glomerulonephritis. With these facts in mind, periodic hematuria and renal insufficiency which developed in the patient cited were probably due to an exacerbation of glomerulonephritis, secondary to the bacteremia, and renal tissue rendered hypersensitive to any foreign, intravenously given fluid. This combined cause of hematuria was noted often in the glomerulonephritis, so-called trench nephritis, of soldiers in World War I. Regardless of the cause of the renal dysfunction in this patient, further use of antibiotics, if bacteremia recurs, is indicated, but during their administration renal function should be carefully watched. In renal disease, a concentration of urea in the blood of 100 mg. per 100 cc. can be a danger signal. Even with renal dysfunction of this degree, further antibiotic therapy is not contraindicated if increasing renal dysfunction does not take place.

CHOLESTEROL CONTENT OF FOODS

To the Editor:—*Please supply the cholesterol content of foodstuffs, including shellfish.*

K. P. A. Taylor, M.D., Clearwater, Fla.

Answer.—The following table summarizes the cholesterol content of common foods. It is taken from the book, "Nutrition and Diet in Health and Disease," by McLester and Darby. It should be remembered that dietary cholesterol per se is not involved in the formation of blood cholesterol.

*Cholesterol Content of Foods**

Food	Total Cholesterol Level, Mg./100 Gm.
Muscle meat	
Beef round (medium fat)	125
Beef round (lean)	95
Veal shank	140
Veal breast	100
Pork spareribs	105
Rabbit	50
Chicken (light)	90
Chicken (dark)	60
Duck	70
Pigeon	110
Variety meats	
Liver	
Lamb	610
Pork	420
Beef	320
Calf	360
Heart (beef)	145
Kidney (beef)	405
Sweetbread	280
Tripe	150
Egg products	
Egg yolk	2,000
Fresh whole egg	468
Dairy products	
Fresh Jersey milk (3.7% fat)	24
Fresh Holstein milk (2.5% fat)	19
Butter	280
Cheese, American	160
Cheese, Swiss, processed	145
Cheese, Monterey Jack	190
Casein, raw	65
Fish and seafood	
Oysters, eastern	230‡
Oysters, California	280-470‡
Crab	145‡
Tuna †	149-172
Mackerel †	240
Sardines †	190
Codfish	50
Salmon	60
Shrimp	150
Turtle	70
Brewer's yeast, dry	680‡

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* Based chiefly on compilation by Okey (*J. Am. Dietet. A.* 21:341, 1945, and personal communication).

† Geiger, *J. A. M. A.* 139:194 [Jan. 15] 1949.

‡ Total digitonin precipitable sterol. These foods contain sterols other than cholesterol.

Cholesterol is formed in the intermediary metabolism from many substances, and any dietary constituents may act as its precursor. Since dietary cholesterol is found in animal foods of great nutritive value (meat, milk, and eggs), it is unwise at the present state of knowledge to cut down or cut out the consumption of such foods.

CALCIUM AND IODINE INTAKE

To the Editor:—*A 40-year-old patient has been taking one capsule three times a day (not prescribed by a physician) containing 0.5 Gm. of dicalcium phosphate and 400 units of vitamin D. He has also been taking one tablet three times a day containing 0.3 mg. of iodine and one multiple vitamin capsule daily for several years. He drinks about one glass of milk a day. He states that he feels fine all the time, but recently some of his friends have warned him that he is taking too much calcium and iodine. Are there any harmful effects of this much calcium or iodine over a long period of time?*

A. M. Earle, M.D., Charleston, W. Va.

Answer.—Apparently, adaptation to wide ranges of calcium intake is possible without observable effects. The amount of calcium that would be obtained from the three dicalcium phosphate capsules would be about 390 mg. This amount is slightly less than one-half the recommended dietary allowance of the Food Nutrition Board. One would certainly not expect a toxic reaction from this amount. According to the National Research Council, the average intake of iodine is about 150 mcg. per day. The ingestion of three capsules per day containing 300 mcg. of iodine would mean that almost 1 mg. of iodine per day would be ingested. This is far below the toxic dose.

According to Sollmann's "Manual of Pharmacology," the fatal dose of iodine is usually 2 to 3 Gm. Individually there may be great variations in iodine intake, but generally the thyroid is able to compensate for these changes and maintains a normal rate of secretion of thyroxin. The amount of calcium and iodine obtained from the product described would, therefore, not be harmful.

PENICILLIN ALLERGY

To the Editor:—*Please outline the emergency treatment of anaphylaxis due to an injectible drug such as penicillin. Given an anaphylactic response, what is the prognosis with and without treatment? How soon is it safe to leave a patient unobserved after giving a potentially allergenic material? Are antibiotics more allergenic when given intramuscularly than when given by mouth? Is the availability of oxygen essential in the treatment of anaphylaxis?*

Charles A. Tompkins, M.D., Tucson, Ariz.

Answer.—An anaphylactic reaction to penicillin is manifested immediately by generalized urticaria, dizziness, cyanosis, tightness in the chest, circulatory collapse, pulmonary edema, shock, and, frequently, death. The emergency treatment includes administration of oxygen, digitalis, antihistaminics by injection, a 1:1,000 solution of epinephrine subcutaneously and/or intravenously, and the intravenous administration of ACTH or hydrocortisone. Symptomatic therapy is included. The prognosis is usually grave if one is confronted with a severe anaphylactic reaction. Controls are not available, but most authorities believe that patients do better with than without treatment. Patients are usually observed for a period of 30 minutes after receiving an injection of a potentially allergenic material. Reactions occur much more rapidly and may be more serious when the antibiotic is administered parenterally than when given by mouth, although deaths have been reported from the oral administration of penicillin. Oxygen should be made available in the treatment of a reaction.

POSTVACCINAL ENCEPHALITIS

To the Editor:—*If outdated smallpox vaccine was used on a child and the child subsequently developed encephalitis, could there be any causal relationship between the vaccine and the encephalitis?* *M.D., New York.*

Answer.—The correspondent's letter does not state what type of reaction (primary, vaccinoid, immune, or no take) the subject experienced after vaccination with the outdated vaccine or whether the child had had a previous successful vaccination. The cause of postvaccinal encephalitis is unknown, but the occurrence of the disease is at least mediated by inoculation of viable vaccinia virus. Outdated vaccine, if inactive, would not be expected to cause postvaccinal encephalitis. If, in the case described, there was no evidence of a take, it is extremely unlikely that the vaccination had anything to do with the encephalitis. The only hazard from use of outdated smallpox vaccine is that it may not contain viable vaccinia virus and, hence, may be incapable of inducing immunity. Outdated vaccine which has been properly stored (at temperatures below 0 C) may still be potent and carry the usual risk of postvaccinal complications.

CIRCUMCISION AND CANCER

To the Editor:—*Could circumcision in a man past 30 years of age cause carcinoma of the penis? Would it be poor medical practice to perform circumcision on men past that age for whom the cause is not urgent?*

R. E. Dallas, M.D., Thomaston, Ga.

Answer.—The primary purpose of circumcision is better hygiene of the male genitalia. Since carcinoma of the penis is almost unheard of in circumcised peoples, it is believed that carcinoma is due to chronic irritation of smegma and poor hygiene. Circumcision would not cause carcinoma. Adequate circumcision is indicated whenever there is chronic irritation or difficult retraction of the foreskin regardless of the patient's age. It would be poor practice to jeopardize the health of a patient by waiting to see what will happen. Circumcision is a minor operation which can be performed with use of local anesthesia without difficulty, and it certainly does not cause cancer or impotence.

ALOPECIA TOTALIS

To the Editor:—*A 25-year-old, well-developed woman of normal intelligence with normal fingernails has a complete lack of hair over her entire body, including the eyelashes. She delivered a full-term normal boy with a normal hair distribution. The patient's mother and father are apparently normal. Of six siblings, three girls, including the patient, exhibit complete lack of hair. What are the probabilities of this trait being transmitted to the patient's son? What are the probabilities of hairlessness in his progeny? Aside from three hairless siblings in the family, there is no other family history of alopecia.*

Everett L. Holt, M.D., Corpus Christi, Texas.

Answer.—The inheritance of alopecia has been reported as a dominant, a recessive, and a sex-linked recessive trait. In the patient in question, two normal parents have six children, three of whom have alopecia totalis. No other history of the trait is found in the family. It would seem that in this case the trait occurs as a simple Mendelian recessive. If the affected woman did not marry one of her relatives, it is doubtful that any of her children will show the trait. Since the trait is rare, the chances are remote that it will occur again in the family for many generations, provided relatives do not marry each other. Each child of the affected persons, however, will carry the defective gene. When two normal people carrying the defective gene have a child, the chances are one in four that it will be hairless.

PENICILLIN REACTIONS

To the Editor:—*Is there a definite relationship between the total dosage of penicillin given and the incidence of reactions to penicillin, other factors being equal?* *M.D., Massachusetts.*

Answer.—This question can be answered with an unequivocal "no." About 10% of the population may become sensitive to a food, drug, cosmetic, or other substance during their lifetime. The remaining 90% fail to become sensitive to antigenic substances regardless of the number of contacts with them. Among the 10% who are prone to become sensitive to antigenic substances, there is a great variation in their resistance to sensitization. In the case of penicillin, some persons acquire sensitivity after a single contact with the drug while others require two or more contacts. Cases have been reported in which apparently no known contact with penicillin could be demonstrated and yet a relatively violent reaction occurred on injection of this drug. On the other hand, some patients have had several hundred injections of penicillin before sensitivity developed. Anaphylactoid reactions have followed skin testing with penicillin, the sucking of a single penicillin troche, or the ingestion of a single penicillin tablet. Serious reactions have also followed administration of poliomyelitis vaccine, even though the finished vaccine contains only a minute amount of penicillin. Pelner (*New England J. Med.* 260:230, 1959) has described allergic reactions to poliomyelitis vaccine.

VOLATILE COMPOUNDS AND GLAUCOMA

To the Editor:—*A 15-year-old boy has failing vision. He had never had any ocular complaint previously. The left eye was myopic, taking about a —1.00 diopter to bring the vision to 20/20. The right eye had far advanced glaucoma with only a small segment of the lateral field remaining. Pressure in the right eye was 65 and in the left 24 mm. Hg. The patient works, as a hobby, with plastic wood containing such volatile compounds as alcohol, acetone, isopropylacetone, and toluene. Is it possible that these have caused the glaucoma? For the good of the other eye should he refrain from working with such products?*

L. Philip Cox, M.D., Fredericksburg, Va.

Answer.—The volatile compounds mentioned are used in many industries, and there is no evidence that they are related to the cause of glaucoma.

TESTOSTERONE AND SERUM CHOLESTEROL

To the Editor:—*In answer to the question on the effect of testosterone regarding atherogenesis, which appeared in* The Journal, *Jan. 3, 1959, page 96, it is stated: "When used therapeutically, its [testosterone's] effect on serum cholesterol is, for practical purposes, negligible." Taken at face value, this statement is seriously in error: What is meant by "practical purposes"? If by these words it is meant that no change in serum total cholesterol concentration occurs after recommended dosages of testosterone are given, then the statement is correct insofar as the average serum cholesterol level of a group of subjects receiving testosterone is concerned. In 18 subjects receiving 27 courses of a variety of androgens at dosage levels both in excess of and below those amounts generally accepted as necessary for maintenance in the agonadal state, the mean change in serum cholesterol level relative to pretreatment control values was an increase of 1%. However, in these same subjects whose mean serum cholesterol levels were so little influenced by testosterone, a mean reduction in high-density alpha lipoprotein to a value only 47% ± 4% of the control level and an increase in lower-density beta lipoprotein to a value 134% ± 10% of control was noted (Furman and Howard,* Ann. Int. Med. *47:969, 1957).*

In other words, while testosterone may cause little or no change in serum cholesterol levels, as determined by conventional chemical techniques, there is an extraordinary alteration in the form in which this cholesterol exists in the serum or plasma. Since that portion of the serum cholesterol circulating as a high-density lipoprotein is easily reduced 50% by testosterone, with a comparable increase in the cholesterol content of the lower-density lipoprotein, it is misleading to say that the effect of testosterone on serum cholesterol is negligible.

The clinical significance of such testosterone-induced changes in the physical state of the serum lipids is not yet unequivocally established, but there is impressive and increasing evidence that coronary and cerebral atherogenesis is related to the amount of cholesterol circulating as a lower-density lipoprotein and that the disease develops more rapidly and is clinically manifest earlier in subjects in whom the ratio of high-density (alpha) to lower-density (beta) lipoproteins is low (Jencks and others, J. Clin. Invest. *35:980, 1956; Furman and others,* Am. J. Med. *24:80, 1958; Furman and others,* Circulation *17:1076, 1958).*

Robert H. Furman, M.D.
Head of Cardiovascular Section
Oklahoma Medical Research Foundation.

The above comment was referred to the consultant who answered the original question, and his reply follows.—Ed.

To the Editor:—*This consultant believes that the Oklahoma physician is confusing the whole issue. The answer as initially stated is correct for the practicing physician. The excessive dietary ingestion of butterfats and various other animal fats by Americans today has more bearing on atherogenesis than the therapeutic use of testosterone. Reevaluation of all clinical and experimental data of testosterone in the human being, particularly as concerns its relation to various diets, is necessary before incriminating a naturally occurring hormone in the male. Therefore, at this comparatively early stage of study of the possible relationship of testosterone to atherogenesis, let us not become alarmists and prematurely suggest a complete change in our dietary habits, leave untreated the agonadal male, and perhaps castrate or treat with estrogens all males even before they have fulfilled their reproductive roles.*

WASHINGTON NEWS

Committee Meets on Aging Problems . .
A. M. A. Proposes Medical Assistance Plan . .
Keogh Bill Hearings Set in Senate . .
Auto Safety Hearings Set . .
Administration Asks Changes on Research Bill . .

ADVISORY COMMITTEE ON AGING MEETS TO DRAFT PLANS FOR WHITE HOUSE CONFERENCE

The Advisory Committee to the White House Conference on Aging held its first formal session here and heard officials urge an "action" program to help meet the problems of the nation's elderly population.

The 130-member group, composed of federal and private experts in all fields involving the aging, is assigned the task of making plans and preparations for the conference, which will be held in 1961. The conference is intended to come up with a broad program to relieve the economic, medical, psychological, and other problems of the rapidly expanding number of elder persons.

Addressing the group at its first meeting in the Department of Health, Education, and Welfare, John B. Martin Jr., chairman of an advisory subcommittee on organization, declared that the conference will be a success only if it spurs widespread action at the local level.

HEW Secretary Arthur S. Flemming emphasized the magnitude and scope of the task confronting the group, noting that there are almost 50 million Americans 45 years of age or older.

Robert W. Kean, chairman of the Advisory Committee, said he was confident it will "be a working group which will meet the challenge that has been set for it." Mr. Kean said he hoped the conference would provide a valuable guideline to Congress in the legislative field. Congress' interest in the problem is pointed up by the fact that there are some 500 bills before the House and Senate now dealing with various aspects of social security, he said.

The following subcommittees and their chairmen were named by Mr. Kean:

Attendance and Selection of Delegates—Michael A. Stepovich, former territorial governor of Alaska.

National Organization—Viola Hynes, president of the National Council of Jewish Women.

Organization of Subject Matter, Procedure, and Theme—John B. Martin Jr., chairman of the Michigan State Legislative Advisory Committee on Problems of the Aging.

Program Organization and Arrangements—Robert Blue, former governor of Iowa.

Publicity—Joseph C. Buckley, a member of the Connecticut commission on services to elderly persons.

State and Local Action—Grace J. Schell, chairman of the Governor's State Committee on Aging in Arizona.

A. M. A. PRESENTS CONGRESS VIEWS ON SOCIAL SECURITY OPERATIONS

The American Medical Association proposed that Congress consider allowing the states to combine into one program the current four public assistance medical programs. There are now four separate programs covering the needy blind, aged, dependent children, and permanently and totally disabled.

In a letter to Rep. Burr P. Harrison (D., Va.), Dr. F. J. L. Blasingame, A. M. A. Executive Vice-president, said that a single medical program administered by a single agency "would help to eliminate waste, confusion and duplication resulting from the present multiplicity of programs." Furthermore, he said, a uniform program "would tend to promote higher quality medical care."

Representative Harrison heads a House ways and means subcommittee on administration of the social security laws.

Dr. Blasingame noted in his letter that the A. M. A. House of Delegates last December recommended that the Social Security Act be amended to permit the states to combine the programs.

At present, Dr. Blasingame said, public assistance recipients under different programs in the same state are frequently eligible for radically different levels of medical care.

The A. M. A. official also suggested congressional consideration of whether the medical staff of the Bureau of Public Assistance "is sufficient to provide adequate counseling to the states on changes in their individual programs . . .," and whether "sufficient liaison has been maintained with the various professional organizations actually providing medical care."

Another suggestion was that a special medical advisory committee might be established in view of the fact that there are no physicians on the recently appointed Social Security Advisory Committee.

KEOGH BILL HEARINGS SET IN SENATE

Legislation to encourage the self-employed, such as physicians, to invest in pension and retirement plans was scheduled for hearings before the Senate Finance Committee June 17 by Chairman Harry F. Byrd (D., Va.).

The main measure before the committee is the bill sponsored by Rep. Eugene J. Keogh (D., N. Y.) and Rep. Richard M. Simpson (R., Pa.) that won overwhelming House approval earlier this session. The legislation authorizes tax deferrals of up to 10% of adjusted gross income, not to exceed $2,500 annually, for self-employed persons who put this money into pension plans. The aim is to provide the self-employed with tax treatment similar to that granted employed persons whose contributions to pension plans are not taxable.

Sen. George Smathers (D., Fla.), a high-ranking member of the Finance Committee, has introduced a measure almost identical to the bill that cleared the House. However, the Smathers measure would not go into effect until the taxable year 1960. The senator said this should soften the arguments of those who might be opposed to the legislation on grounds it would unbalance the budget this year.

HEARINGS SET ON AUTO SAFETY BILL

A House interstate and foreign commerce subcommittee scheduled hearings starting July 7 on legislation to require auto manufacturers to install safety equipment in cars sold to the federal government. The measure is sponsored by Rep. Kenneth Roberts (D., Ala.), chairman of the subcommittee. The aim is to spur the manufacturers to install the equipment in all autos, since the federal government is a large buyer. Under this legislation the Secretary of Commerce would determine what safety features should go into cars purchased by the government. The Department of Health, Education, and Welfare recently ordered seat belts installed in all department vehicles.

ADMINISTRATION URGES CHANGES IN MEDICAL RESEARCH MEASURE

The administration stepped up its opposition to the Senate-passed bill establishing a new National Institute of Health to promote international medical research. Despite overwhelming Senate approval of the legislation Arthur S. Flemming, Secretary of Health, Education, and Welfare, said he will "press vigorously" to have the House write in administration changes.

As of this writing, hearings on the bill had not been slated by the House Interstate and Foreign Commerce Committee.

The administration endorsed the objectives of the measure but opposed specific provisions of the legislation as it cleared the Senate, especially the 50 million dollar annual authorization.

Other administration proposals that the Senate did not accept would place all authority for the program under the President, rather than the surgeon general of the Public Health Service, and would remove the mandatory establishment of a new national institute.

GRANTS TO PUBLIC HEALTH SCHOOLS

The Public Health Service awarded $450,000 of grants to help finance specialty training in public health for physicians, nurses, engineers, and other personnel employed in government health agencies.

The grants went to the nation's 11 schools of public health. About 20,000 professional public health agency personnel in the United States need additional training in modern methods for the investigation and control of disease and the maintenance of a healthful environment, the PHS said. The 11 schools are at the following universities: California (Berkeley), Columbia, Harvard, Johns Hopkins, Michigan, Minnesota, North Carolina, Pittsburgh, Puerto Rico, Tulane, and Yale.

FDA PROPOSES MORE DATA FOR PHARMACISTS

The government moved to encourage drug manufacturers to send pharmacists indications and dosages for prescription drugs. This would help pharmacists check against possible mistakes in prescriptions, the Food and Drug Administration said in a policy statement, noting that there are no regulations preventing drug makers from supplying such data. "Obviously, such printed matter should not be displayed to prospective purchasers to promote over-the-counter sale of prescription drugs," said a representative. However, drug companies "should be encouraged to supply such printed matter to the pharmacist for his professional information," the agency said.

HOUSE APPROVES WATER POLLUTION MEASURE

The House passed and sent to the Senate legislation doubling the size of the federal program to help states and localities combat pollution of rivers.

The measure, authorizing spending of 100 million dollars annually of federal grants, was approved by a 254 to 142 vote, despite Republican warnings that it would unbalance the budget and might face a presidential veto. The ceiling on a federal grant for an individual project would be raised from $250,000 to $500,000 under the bill, but the federal share could not exceed 30% of the project's total cost.

A Republican effort to require states to match dollar for dollar the federal contribution—now outright grants—was unsuccessful.

MISCELLANY

Clostridium perfringens, a type of bacteria little known in the U. S., was identified by PHS as the cause of the food poisoning outbreak that struck 100 delegates to a labor meeting in Washington, D. C. The agency said the finding "has led to speculation as to whether it may be a frequent cause of food poisoning in the United States."

Pro-Banthīne®...what it will do and what it will not do...in Peptic Ulcer

Much consideration has been devoted recently to a reappraisal of the role of anticholinergic drugs in the management of peptic ulcer.

Such reappraisal has presented no difficulties at Searle. At no time have we suggested that Pro-Banthīne should be substituted for antacids, rest, psychotherapy or even common sense in managing the patient with peptic ulcer.

Action of Pro-Banthīne:

The action of Pro-Banthīne (brand of propantheline bromide) is simple and its effects, allowing for the variability of the human estate, are predictable. Pro-Banthīne competes with and, in competing, inhibits the action of acetylcholine. This competition is highly effective at parasympathetic effector sites and, except with high dosage, somewhat less so at the autonomic ganglia.

Since parasympathetic nerves are motor and secretory to the stomach and motor to the intestines, Pro-Banthīne reduces both motility and secretions in the stomach and motility in the intestines. These actions have often been demonstrated experimentally and clinically.

What It Does:

Relieves Pain—One of the natural consequences of the actions of Pro-Banthīne is to reduce or to eliminate pain in peptic ulcer. Whether the pain is attributable to acid, to excessive motility or, to steer a middle course, to spasm induced by acid, the pronounced inhibitory effect of Pro-Banthīne on both secretion and motility might be expected to suppress the characteristic distress of ulcer.

In point of fact, relief of pain is one of the most prominent effects of Pro-Banthīne in peptic ulcer. Phrases such as "unexcelled" and "almost invariably effective" dot the literature referring to it.

Reduces Acidity—Since reduction of acid and rest for the hypermotile stomach and duodenum are accepted means of supporting the regenerative processes of the gastroduodenal mucosa, the physiologic modifications induced by Pro-Banthīne should be expected to have therapeutic implications in the healing of ulcers also. They do. Not only does Pro-Banthīne reduce gastric acid and motility but, through these actions, it also potentiates and prolongs the neutralizing property of antacids.

Aids Healing—Schwartz, Lehman, Ostrove and Seibel prescribed 120 to 180 mg. of Pro-Banthīne daily for 129 ulcer patients and found definite evidence, both clinical and roentgenographic, of accelerated healing.

With high doses (270 to 330 mg. daily) Barowsky, Schwartz and Lister reduced the mean duration of treatment in twenty-five patients with refractory ulcers from 135 to 17 days.

Helps Prevent Recurrences—Much the same considerations argue for the value of Pro-Banthīne in holding the reactivation of healed ulcers in abeyance, but the difficulty of regulating the diet, medication and mode of living of ulcer patients over long periods of time makes assessment of the role of Pro-Banthīne in preventing recurrences difficult. Nevertheless, in a study of 250 patients with established patterns of recurrence Texter and associates found that patients maintained on methantheline, less potent analogue of Pro-Banthīne, had significantly fewer recurrences than a control series taking atropine.

Schwartz and his co-workers considered freedom from symptoms when recurrences would be expected, together with tolerance and relief of symptoms, as a standard in establishing successful treatment in 118 of 129 patients.

Provides Selective Action—In inhibiting the action of acetylcholine in the stomach and intestines Pro-Banthīne also, though to a lesser extent, influences other cholinergically activated organs. That this influence sometimes leads to such secondary effects as dryness of the mouth, blurring of vision and hesitancy of urination is well known and bears consideration. It is one of the distinct advantages of Pro-Banthīne that it acts more effectively on the gastrointestinal tract than elsewhere. Secondary effects usually disappear during the course of treatment and only rarely limit therapy.

Evidence of selective action has been recorded by several investigators, but the most interesting confirmation of this selectivity was reported by Barowsky, Schwartz and Lister. They prescribed 30 to 45 mg. of Pro-Banthīne every hour and a half, except for the hour before and the hour following meals, for their patients with refractory ulcers. They were surprised and gratified by how few anticipated side reactions materialized. No serious toxic effects or side reactions occurred. The incidence of good response on double or triple the usual doses rose from 31 to 88 per cent.

Lowers Incidence of Failures—Variable results might be anticipated in a disease in which the psychic component plays such a large part and, of course, response to treatment does vary in patients with peptic ulcer. Observations of Lichstein and associates show that the 11 per cent of their patients who failed to respond to Pro-Banthīne had deeply ingrained anxiety on a psychoneurotic basis.

Successful management of such patients may well depend more on the patient's intelligence, the modification of his social environment and the skill of his physician in psychotherapy than on any medication. However, the successful experience of Barowsky and his colleagues in using large, frequent doses of Pro-Banthīne in patients with refractory ulcers might be borne in mind before Pro-Banthīne is abandoned as ineffective. Also worthy of trial in these patients is Pro-Banthīne® with Dartal® (brand of propantheline bromide with thiopropazate dihydrochloride), which combines the outstanding anticholinergic action of Pro-Banthīne with the highly efficient tranquilizing action of Dartal.

What It Will Not Do:

There are aspects of the medical management of peptic ulcer in which Pro-Banthīne has no demonstrable benefit. There is no reliable evidence that Pro-Banthīne reduces the incidence of complications or the need for surgery.

It will not abolish the obligation of physicians to evaluate each patient individually and to modify therapeutic measures to each patient's requirements. Nor will it do away with the necessity for the patient to regulate his life to the demands of his disease. But the modifying action of Pro-Banthīne on the physiologic activity of the gastrointestinal tract and its beneficial effects on the course of peptic ulcer have been established by too many investigators to be seriously questioned. Wisely used in conjunction with other standard therapeutic measures, Pro-Banthīne can inhibit pain, hasten healing and space out the intervals of peptic ulcer recurrence and do so without serious discomfort to the patient.

G. D. Searle & Co., Chicago 80, Illinois. Research in the Service of Medicine.

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Texter, E. C. [illegible] Peptic Ul [illegible] Adjunct t [illegible] 11:1062 (Nov.) 1953.

MEETINGS

AMERICAN MEDICAL ASSOCIATION: Dr. F. J. L. Blasingame, 535 North Dearborn St., Chicago 10, Executive Vice-President.
1959 Clinical Meeting, Dallas, Texas, Dec. 1-4.
1960 Annual Meeting, Miami Beach, Fla., June 13-17.
1960 Clinical Meeting, Washington, D. C., Nov. 29-Dec. 2.
1961 Annual Meeting, New York City, June 26-30.
1961 Clinical Meeting, Denver, Nov. 28-Dec. 1.

AMERICAN

1959

June

Air Pollution Control Association, Hotel Statler, Los Angeles, June 22-26. Mr. Harry M. Pier, 4400 Fifth Ave., Pittsburgh 13, Executive Secretary.

American Physical Therapy Association, Hotel Leamington, Minneapolis, June 21-26. Miss Annetta Cornell Wood, 1790 Broadway, New York 19, Executive Director.

Intermountain Pediatric Society, Sun Valley, Idaho, June 26-28. Dr. J. R. Newton, Memorial Medical Center, 2000 S. 9th E., Salt Lake City, Utah, Publicity Chairman.

Maine Medical Association, The Samoset, Rockland, June 21-23. Dr. Daniel F. Hanley, P. O. Box 240, Brunswick, Executive Director.

Society of Nuclear Medicine, Palmer House, Chicago, June 18-20. Dr. Morris T. Friedell, 104 S. Michigan Ave., Chicago 3, Chairman, Press & Public Relations Committee.

South Dakota State Medical Association, Sheraton Johnson Hotel, Rapid City, June 20-23. Mr. John C. Foster, 300, 1st National Bank Bldg., *Sioux Falls, Executive Secretary.*

Upper Peninsula Michigan Medical Society, Gateway, Land of Lakes, Wis., June 19-20. Dr. Richard D. Cecconi, Iron Mountain, Mich., Secretary.

July

American Society of Facial Plastic Surgery, New York City, July 17. Dr. Samuel M. Bloom, 123 E. 83rd St., New York 28, Secretary.

American Society of X-ray Technicians, Shirley Savoy Hotel, Denver, *July 4-9. Miss Genevieve J. Eilert,* 16 14th St., Fond du Lac, Wis., Executive Secretary.

Oregon Cancer Conference, University of Oregon Medical School, Portland, July 16-17. Dr. Martin A. Howard, 1115 S. W. Taylor St., Portland 5, Ore., Chairman.

Rocky Mountain Cancer Conference, Brown Palace Hotel, Denver, July 22-23. Dr. N. Paul Isbell, 835 Republic Bldg., Denver 2, Chairman.

August

American Congress of Physical Medicine and Rehabilitation, Hotel Leamington, Minneapolis, Aug. 30-Sept. 4. Miss Dorothea C. Augustin, 30 N. Michigan Ave., Chicago 2, Executive Secretary.

American Dietetic Association, Statler Hilton, Los Angeles, Aug. 25-28. Miss Ruth M. Yakel, 620 N. Michigan Ave., Chicago 11, Executive Secretary.

American Hospital Association, Statler Hotel, New York City, Aug. 24-27. Dr. Edwin L. Crosby, 18 E. Division St., Chicago, Director and Secretary.

American Veterinary Medical Association, Hotel Muehlebach, Kansas City, Mo., Aug. 24-28. H. E. Kingman Jr., D.V.M., 600 S. Michigan Ave., Chicago 5, Executive Secretary.

Biological Photographic Association, Inc., Sheraton-Mount Royal Hotel, Montreal, Canada, Aug. 31-Sept. 3. Miss Jane H. Waters, Box 1668, Grand Central P. O., New York 17, Executive Secretary.

National Medical Association, Detroit, Aug. 10-13. Dr. John T. Givens, 1108 Church St., Norfolk, Va., Secretary.

Nevada State Medical Association, Reno, Aug. 19-22. Dr. Gilbert G. Lenz, 505 S. Arlington Ave., Reno, Nev., Chairman.

Rocky Mountain Radiological Society, Shirley-Savoy Hotel, Denver, Aug. 20-22. Dr. John H. Freed, 4200 E. Ninth Ave., Denver 20, Secretary-Treasurer.

Society for Clinical and Experimental Hypnosis, Fairmont Hotel, San Francisco, Aug. 3-5. Dr. Irving Schwartz, 2340 Sutter St., San Francisco 15, Chairman, Program Committee.

West Virginia State Medical Association, The Greenbrier, White Sulphur Springs, Aug. 20-22. Mr. Charles Lively, P. O. Box 1031, Charleston 24, Executive Secretary.

September

American Association of Medical Clinics, Sheraton-Blackstone Hotel, Chicago, Sept. 24-26. Dr. Edwin P. Jordan, Box 58, Charlottesville, Va., Executive Secretary.

American Association of Obstetricians and Gynecologists, The Homestead, Hot Springs, Va., Sept. 10-12. Dr. E. Stewart Taylor, 4200 E. Ninth Ave., Denver 20, Secretary.

American Association for the Surgery of Trauma, Mount Washington Hotel, Bretton Woods, N. H., Sept. 24-26. Dr. William T. Fitts Jr., 3400 Spruce St., Philadelphia 4, Secretary.

American College of Gastroenterology, Biltmore Hotel, Los Angeles, Sept. 19-26. Mr. Daniel Weiss, 33 W. 60th St., New York 23, N. Y., Executive Director.

American College of Surgeons, The Traymore Hotel, Atlantic City, N. J., Sept. 28-Oct. 2. Dr. Paul R. Hawley, 40 E. Erie St., Chicago 11, Director.

American College of Surgeons, Ohio Chapter, Statler Hotel, Cleveland, Sept. 11-12. Dr. Berton M. Bogle, 311 S. Market, Troy, Ohio, Secretary-Treasurer.

American Roentgen Ray Society, The Netherland Hilton Hotel, Cincinnati, Sept. 22-25. Dr. C. Allen Good, Mayo Clinic, Rochester, Minn., Secretary.

American *Society* of Clinical *Pathologists*, The Palmer House, Chicago, Sept. 7-11. Mr. Claude E. Wells, 2052 N. Orleans, Chicago 14, Executive Secretary.

Central Association of Obstetricians and Gynecologists, Drake Hotel, Chicago, Sept. 24-26. Dr. Edwin J. DeCosta, 104 S. Michigan Ave., Chicago 3, Secretary.

College of American Pathologists, The Palmer House, Chicago, Sept. 6. Dr. Arthur H. Dearing, Suite 2115, Prudential Plaza, Chicago 1, Executive Director.

Colorado State Medical Society, Brown Palace and Shirley Savoy *Hotels, Denver, Sept. 8-11.* Mr. Harvey T. Sethman, 835 Republic Bldg., Denver 2, Executive Secretary.

International College of Surgeons, Tennessee Section, Chattanooga, Sept. 28-29. Dr. William G. Stephenson, Medical Arts Bldg., Chattanooga, Tenn., Regent.

Kentucky State Medical Association, Columbia Auditorium, Louisville, Sept. 22-24. Mr. Joseph P. Sanford, 1169 Eastern Pkwy., Louisville 17, Ky., Executive Secretary.

Maryland, Medical and Chirurgical Faculty of the State of, Semiannual Meeting, Ocean City, Sept. 18. Mr. John Sargeant, 1211 Cathedral St., Baltimore 1, Executive Secretary.

Medical Progress Assembly, Tutwiler Hotel, Birmingham, Ala., Sept. 13-15. Dr. Herbert H. Thomas, 920 S. 19th St., Birmingham, Ala., Chairman, Publicity Committee.

Michigan State Medical Society, Pantlind Hotel, Grand Rapids, Sept. 28-29, Oct. 1-3. Mr. William J. Burns, 606 Townsend St., Lansing 15, Mich., Executive Secretary.

Mid-Continent Psychiatric Association, Holiday Inn Motor Hotel, St. Louis County, Mo., Sept. 18-20. Dr. W. Payton Kolb, Baptist Medical Arts Bldg., Little Rock, Ark., Secretary.

Montana Medical Association, Finlen Hotel, Butte, Sept. 17-19. Mr. L. Russell Hegland, 1236 N. 28th St., Billings, Mont., Executive Secretary.

National Recreation Congress, Morrison Hotel, Chicago, Sept. 28-Oct. 2. Mr. Jesse Reynolds, Department of Recreation and Parks, The Mosque, Laurel and Main Streets, Richmond 20, Va., Chairman.

North American Federation, International College of Surgeons, Chicago, Sept. 13-17. For information write the Secretariat, 1516 Lake Shore Dr., Chicago 10.

Oregon State Medical Society, Medford Hotel, Medford, Sept. 23-25. Mr. Roscoe K. Miller, 1115 S. W. Taylor St., Portland 5, Ore., Executive Secretary.

Tennessee Valley Medical Assembly, Chattanooga, Tenn., Sept. 28-29. Dr. Guy M. Francis, 109 Medical Arts Bldg., Chattanooga 2, Tenn., Chairman.

United States Section, International College of Surgeons, Palmer House, Chicago, Sept. 13-17. Dr. Ross T. McIntyre, 1516 Lake Shore Dr., Chicago 10, Executive Secretary.

Utah State Medical Association, Hotel Utah Motor Lodge, Salt Lake City, Sept. 16-18. Mr. Harold Bowman, 42 S. 5th East, Salt Lake City 2, Executive Secretary.

Washington State Medical Association, Olympic Hotel, Seattle, Sept. 13-16. Mr. Ralph W. Neill, 1309 Seventh Ave., Seattle 1, Executive Secretary.

World Medical Association, Montreal, Canada, Sept. 7-12. Dr. Louis H. Bauer, 10 Columbus Circle, New York 19, Secretary-General.

October

Academy of Psychosomatic Medicine, Sheraton-Cleveland Hotel, Cleveland, Oct. 15-17. For information write: Dr. Bertram B. Moss, Suite 1035, 55 E. Washington St., Chicago 2, Secretary.

American Academy of Ophthalmology and Otolaryngology, The Palmer House, Chicago, Oct. 11-16. Dr. William L. Benedict, 15 Second St., S. W., Rochester, Minn., Executive Secretary.

American Academy of Pediatrics, The Palmer House, Chicago, Oct. 5-8. Dr. E. H. Christopherson, 1801 Hinman Ave., Evanston, Ill., Executive Secretary.

American Association of Medical Assistants, Benjamin Franklin Hotel, Philadelphia, Oct. 16-18. Mrs. Stella Thurnau, 510 N. Dearborn, Room 924, Chicago 10, Executive Secretary.

American Association of Medical Record Librarians, Radisson Hotel, Minneapolis, Oct. 12-15. Miss Margaret G. Scully, 510 N. Dearborn St., Chicago 10, Director.

American College of Chest Physicians, 25th Anniversary Homecoming Meeting, Albuquerque, N. M., Oct. 14-17. Mr. Murray Kornfeld, 112 E. Chestnut St., Chicago 11, Executive Director.

American College of Preventive Medicine, Hotel Ambassador, Atlantic City, N. J., Oct. 21-22. Dr. John J. Wright, P. O. Box 1267, Chapel Hill, N. C., Secretary-Treasurer.

American Heart Association, Trade and Convention Center, Philadelphia, Oct. 23-27. Mr. William F. McGlone, 44 E. 23rd St., New York 10, Secretary.

American Medical Writers' Association, Chase Hotel, St. Louis, Oct. 2-3. Dr. Harold Swanberg, 510 Maine St., Quincy, Ill., Secretary.

American Otorhinologic Society for Plastic Surgery, Inc., Conrad Hilton Hotel, Chicago, Oct. 11. Dr. Joseph G. Gilbert, 75 Barberry Lane, Roslyn Heights, N. Y., Secretary.

American Psychiatric Association, Detroit Divisional Meeting, Hotel Statler, Detroit, Oct. 29-31. Dr. Benjamin Jeffries, 16321 Mack Ave., *Detroit 24, Co-Chairman, Planning Committee.*

American Public Health Association, Convention Hall, Atlantic City, N. J., Oct. 19-23. Dr. Berwyn F. Mattison, 1790 Broadway, New York 19, N. Y., Executive Director.

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USE OF ORALLY ADMINISTERED LIVE ATTENUATED POLIOVIRUSES AS A VACCINE IN A COMMUNITY SETTING

A CONTROLLED STUDY

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Attenuated strains of the three types of poliovirus were used in a study of 550 volunteer subjects. Subjects in group A received a placebo during the first 76 days of the study while those in group B received the polioviruses by mouth; during the remaining days (78th to 139th) group A received the viruses and group B the placebo. No particular type of symptom or reaction marked the entrance of the virus into the body. The children, and to a lesser extent the adults, receiving the virus manifested a generally increased titer of neutralizing antibody. The results for children and adults receiving the placebo were quite different. The positive responses occurred despite the fact that a substantial number of the participants had previously received Salk vaccine. Although the effectiveness of vaccination needs to be demonstrated finally in encounters with the disease itself, this study yielded strong evidence of the effectiveness as well as the safety of the living attenuated poliovirus used.

EFFORTS to develop attenuated living strains of poliovirus for use as immunizing agents against the disease poliomyelitis have been concentrated within the last two decades. The names most prominently associated with these efforts are those of Cox,[1] Koprowski and co-workers,[2] and Sabin.[3] There is strong immunological justification for such attempts. The best and most durable immunity obtainable against a type-specific virus disease is the immunity conferred by an attack of the disease itself, whether such an attack is a full-blown clinical syndrome or a mild, unrecognized, undiagnosed, subclinical infection. It is also a fact that the best immunizing agents now available against virus diseases are the living but modified viruses of smallpox and yellow fever. Veterinary medicine can add numerous similar examples. The aim then is to duplicate natural infection and its resulting immunity but to do so with living agents so modified or attenuated that they do not in themselves produce overt clinical disease.

There are inherent difficulties in controlling the formalinization processes involved in the commercial production of inactivated virus vaccine.[4] There has also been the recent admission that the vaccines so produced and currently in use have been of low

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potency.[5] These two facts, together with the encouraging results so far reported for the vaccines composed of living attenuated poliovirus, are additional compelling reasons for the continuance of research in the field of vaccination against poliomyelitis with such living virus agents.

Until two years ago human trials with attenuated poliovirus vaccines were limited to very small groups and these often living in an institutional environment. But, since then and especially in 1958, the scope of human trials has boldly increased until now thousands of individuals have been fed. Mass trials are complete, are in progress, or are being planned for the immediate future in Latin America,[6] Africa,[7] and Asia and Europe.[8] For example, as of March 10, 1959, more than 550,000 persons had been fed at least one type of the strains used in this study. Of these, 250,000 had received all three types.[9] This study adds a mere 550 to the grand total; it has, however, the virtue of having been completely controlled.

TABLE 1.—*Participants at Beginning of Study, by Age and Vaccinal Status (Salk)**

Age, Yr.	No Vaccine	1 Dose	2 Doses	3 Doses	Totals
Children					
Under 1	48	5	5	2	60
1	8	2	26	12	48
2	...	3	12	38	53
3	...	2	4	32	38
4	...	1	2	27	30
5	...	1	3	15	19
6	...	...	1	8	9
7	...	...	...	...	...
8	...	...	...	2	2
9	...	...	...	2	2
10	...	...	...	2	2
Total children Av. age 2.4	56	14	53	140	263
Fathers Av. age 27	43	13	47	43	146
Mothers Av. Age 26	12	10	48	72	142
Totals	111	37	148	255	551

* 149 families.

Materials and Methods

The attenuated strains used in this study were developed under the direction of Dr. Herald R. Cox, director of viral and rickettsial research, Lederle Laboratories Division of the American Cyanamid Company. The type 1 strain started as a mixture of the Sickle and Mahoney strains of type 1 poliovirus. The type 2 strain was adapted from an original MEF-1 type 2. The type 3 strain was developed from virus isolated from a case of nonparalytic poliomyelitis in a one-year-old child and was originally supplied by Dr. John Fox of Tulane University. The growth and pathogenicity characteristics of these modified strains will be adequately described elsewhere.[10]

The strains used in this study are essentially the same as those used by Martins da Silva and his colleagues [11] in a study carried out about one year previously which included only newborn infants and infants under 6 months of age. The results of this first Minnesota study indicated that the type 2 strain was the least effective antigen. Because of this it was decided, for the present study, to double the dose and to feed this strain first. After the type 2 feeding, types 1 and 3 were fed in sequence at three-week intervals. The dosage administered was computed to be 63,000 to 79,000 tissue culture doses for type 1, 100,000 for type 2, and 200,000 for type 3. The vaccine was dispensed in hard gelatin capsules with the virus adsorbed on granular gelatin.

Population Characteristics and Location.—The population chosen for this study consisted of married University of Minnesota students and their children. These families occupied a village site, maintained by the university, in the so-called southeast section of Minneapolis about five minutes' drive from the main campus in that city. The quarters occupied by these families were duplex back-to-back structures of either the Quonset hut, metal barracks, or prefabricated wood types. The village was surrounded by industry and/or vacant space on the north, east, and south. Only to the west was there any residential area. The water supply and sewage facilities were those of the city itself.

The dwelling area comprised six city blocks which were with one exception all adjacent, with each block filled with closely packed double-dwelling units. One tier of blocks was vacant except for the presence of the Village Students Union. This building was the center of a busy communal life. It was a central meeting place with facilities for the purchase of light meals and refreshments and such items as reading materials and toys. In it were held such activities as governing council meetings, community suppers, a nursery school, dancing classes, and, periodically, a well-baby clinic. There were also some recreational facilities and a room reserved for quiet study.

In the village proper there was a great deal of visiting back and forth, with daily coffee parties and the frequent interchange of baby sitters. Housekeeping per se varied from excellent to very poor depending on the temperament of the individual housewife. The entire environment was that of a closely knit, compact settlement that lived in cramped physical quarters on a hairline budget. The intellectual caliber of the villagers, however, was above what one would normally expect from the occupants of an environment such as has been described. The entire study was administered from an office located at the eastern edge of the village.

Participation in the study project was on an entirely voluntary basis. Nor was it required that an entire family unit participate as such. Some families were represented by only a single participant; the largest participating group comprised a family of six individuals. Previous experience with Salk vaccine to any degree was not a bar to participation. The final participating group represented about half of the total village population.

The characteristics of the participating population (at the beginning of the study) with respect to age and vaccinal status with Salk vaccine are shown in table 1. On the basis of age the population divided itself into two groups: a younger group of children mostly under the age of 6 and an adult group composed of the mothers and fathers. The mean age for the children was 2.4 years, for the fathers 27 years, and for the mothers 26 years. Almost half the population had had the recommended three doses of Salk vaccine. The largest contributors to this group were the children over one year of age and the mothers. About one-fifth of the participants had had no Salk vaccine at all. The largest contributors to this group were the children under one year of age and the fathers. There were relatively few persons (37) who had had only one dose of Salk vaccine, and those with two doses were about evenly divided among children, fathers, and mothers. In the main, then, it was the women and children who had received the complete Salk dosage and the men and infants who had had none. All participants had to agree not to take any Salk vaccine for the duration of the study and, so far as is known, this agreement was not broken.

The location of and the population involved in the study were, of course, not completely typical of either a rural or an urban community. Nevertheless, there were distinct operational advantages in working with such a group in such a location. This community yielded a group of participants concentrated in space to an area of six city blocks. The entire area was only a short distance from the laboratories of the Minnesota Health Department on the University of Minnesota campus. The advantages in time and travel when it came to actually administering and supervising the details of the study are immediately obvious. Further, it was felt that this group, more than any other because of training and outlook, could most readily appreciate the implications, both theoretical and actual, that were involved in such a study. How well they responded to all the implications, including even the odious task of collecting frequent stool specimens, will become apparent later.

Goals of Design.—The design of the study was directed toward achieving three experimental conditions: first, the creation of a control group and control period; second, complete and continuous supervision of all participants; and third, freedom from bias in interpreting clinical information and laboratory results.

Control Group and Control Period: To establish a control group and a control period, at the very outset the participating population was divided into two groups on a purely random basis. These groups were designated A and B. The A group was the control or placebo group which received placebo capsules, while the B group received capsules containing the attenuated virus types. The component unit in each group was the family, not the individual. That is, no family contained both placebo-control and virus-fed individuals at the same time; it was entirely placebo or entirely virus-fed. In order that all participants might eventually receive the vaccine, the procedure was reversed for the two groups after the first round of feeding. The sequence of this procedure appears in table 2.

It would be well to accurately delineate here the control period and definitely identify the control population. The control period extended from day 1 through day 76, during which time the A group received placebo material while the B group was virus-fed. This point is delineated on table 2 by a broken line. It is apparent too that the control population would number approximately half of the total population and that the placebo group's antibody picture would be represented by the results of the antibody titrations on their first two blood specimens. Since, after the control period, the placebo group was in turn virus-fed, the ultimate measure of the vaccine's effect with respect to serum antibody response would include the entire participating population and would be represented by the results of antibody titrations on the first and third blood specimens of everyone in both groups A and B.

TABLE 2.—*Chronology of Orally Administered Poliomyelitis Vaccine Study*

	Group A			Group B		
Day*	Bleedings	Stool Specimens	Feedings	Bleedings	Stool Specimens	Feedings
1- 6	1st			1st		
3- 11		1st			1st	
8- 13			Placebo			Type 2
28- 36		2nd			2nd	
35- 41			Placebo			Type 1
49- 59		3rd			3rd	
57- 62			Placebo			Type 3
70- 79		4th			4th	
71- 76	2nd			2nd		
78- 83			Type 2			Placebo
91- 99		5th			5th	
96-102			Type 1			Placebo
112-121		6th			6th	
116-122			Type 3			Placebo
134-139	3rd			3rd		

* Day 1 is Jan. 27, 1958. Days for stool specimen receipt and feeding overlap, but no family was given capsules until its stool specimens were received.

Supervision: Supervision was effected through a detailed system of record-keeping, through the activities of two public health nurses who were concerned mostly with day-to-day mechanics, and through the maintenance of liaison with the individual families both through the public health nurses and at times with the families' own physicians. Recording of pertinent data was, in general, the responsibility of a specially employed secretary, although the nurses themselves recorded family and individual histories as well as daily progress notes when such were indicated.

Each family had its own data sheet, and each individual participant within a family had his own record sheet. The family sheet contained identifying data for each participating member as well as a listing of the usual daily contacts for each member in the order of frequency with which these contacts were made. In addition there was space for the nurse to note the general state of hygiene, familial and personal, in each case. Records of Salk vaccine status, dates of feeding, and dates of bleeding and stool specimen submission were kept on the family sheet. The results of serum antibody titrations and virus isolation attempts on stool specimens were also recorded on the family form as these became available.

The individual's record sheet was essentially a condensed medical history form listing such items as physician's name and address, previous poliomyelitis history, prior serious illnesses, operations or injuries, and any present disabilities. Pregnancy was noted and the due date of delivery recorded. The immunization history was obtained in some detail, with the date of the last dose of any antigen noted as accurately as possible. A substantial part of the space on the individual record was given over to daily notes and to the recording of symptoms, intercurrent illnesses, and any other information that might be deemed important.

A generalized public health nursing service was offered to all village residents, participating or not. The public health nurses visited each participant's home to complete the family and individual record forms as far as they could. These nurses assisted at bleeding clinics, distributed stool specimen containers, and either fed or supervised the feeding of the capsules. These activities alone brought them into frequent contact with the families. In addition they were subject to call for consultation on any problem that a family wished to discuss with them. Participants were encouraged to report illnesses or symptoms to the public health nurses.

TABLE 3.—*Types of Illness Occurring in Participants During the Control Period**

	Between Feedings 1 and 2 February, %	Between Feedings 2 and 3 February-March, %	Between Feedings 3 and 4 March-April, %
Upper respiratory infections	65.0	18.8	44.8
Gastrointestinal disturbances	18.9	69.2	29.8
Common communicable diseases	4.0	2.3	10.3
Miscellaneous	12.1	9.7	15.1

* 1st half of study.

A letter was sent to the physician named by the participants informing him that the family was taking part in the study. The family physician was further informed that participants were instructed to use ordinary and usual medical facilities for any illness which occurred during the period of the study. In other words, they were urged to consult their own physicians in case of illness. The physician was further invited to use the public health nursing service that had been made available in any manner which he thought convenient and beneficial to the patient and himself. Where no family physician was named, a similar letter was sent to the students' health service of the university.

Freedom from Bias: Only one person in the project team knew the identity of the individuals who comprised the A, placebo-control, group and the B, virus-fed, group. This identity was not divulged until the end of the study period. The participants thus never knew until the end whether and when they had received actual virus or placebo. The project team, with the one exception noted, was in a like position. There could therefore be no bias in the clinical interpretation of symptoms that were reported.

A set of three blood specimens collected at the intervals shown in table 2 was obtained from each participant. These were sent to the laboratory with a label that identified their origin and sequence by code number. All specimens in any one set were always tested on the same day. But, when these sets were actually tested, the original identifying labels had been replaced by a scrambled and random numbering system that made it impossible for the testing personnel to identify any one specimen as to its individual origin, its set origin, or its sequence within any one given set. The laboratory crew who received the specimens, separated the serum, and made the first dilution was different from the crew who did the antibody titrations. Indeed, the two crews worked in different places in the laboratory quarters and there was no overlapping of personnel.

Operation of Study.—The schedule for bleeding, collection of stool specimens, and feeding both placebo and vaccine is set out in detail in table 2. The study got under way on Jan. 27, 1958, and, except for the laboratory work, was completed 140 days later, in June, 1958. This was well in advance of the usual Minnesota poliomyelitis season.

Operations started off by first securing a blood specimen and a stool specimen from each participant. These specimens had to be submitted before virus feeding. About one week was required for each blood specimen collection, each stool specimen collection, and each feeding. The days for stool specimen receipt and feeding overlapped, but no family was fed initially or serially until its entire complement of stool specimens had been received. Reference to table 2 will show that each subsequent feeding in a series was preceded by the collection of a stool specimen, for a total of six such specimens. The second blood specimen was collected between the 71st and 76th days, about the 14th day, on the average, after the third feeding. The third and last blood specimen was collected between the 134th and 139th days, which was some 17 or 18 days, on the average, after the last of the second round of feedings.

The capsules containing either virus or placebo material were delivered to the homes by the public health nurses. Those who could swallow capsule-size medicaments did so. The others, infants and children, were spoon-fed after the capsule contents were mixed with any acceptable liquid. The nurse was thus assured of the ingestion of the material for those at home during the time of her visit. The capsules were left for those not at home, usually the father and sometimes a school child. No attempt was made to relate the feeding to mealtimes.

Certain contraindications to feeding were agreed on in advance. Current vomiting and/or diarrhea were obvious contraindications that demanded a delay in feeding until these symptoms had disappeared. Feeding was delayed for any illness that had a febrile episode until the person's temperature had stabilized itself at a normal range. Open lesions of the oral cavity or the pharynx, whether surgical or due to disease, called for a delay in feeding until these lesions had healed over. Only a single family had to be dropped from the study because of a continuing contraindication. This was a family in which the mother developed considerable dental trouble necessitating frequent extractions. This situation became apparent after one virus feeding, and the family thereafter was assigned placebos for the duration of the study.

Evaluation of Symptoms Occurring During Control Period

Recording and evaluating illnesses and symptoms that occurred during the study period was of paramount importance if the presence or absence of "reaction" symptoms was to be established on a sound basis. During the preliminary phases of the study, it was learned that a good deal of illness could be expected in the village. This was the usual experience. The villagers themselves volunteered that there was always "some kind of cold or flu going around." Pediatricians who had had villagers for patients in the past predicted the usual yearly outbreak of diarrhea.

Table 3 lists illnesses classified under four headings as they occurred between the first and second, the second and third, and the third and fourth feedings. These time intervals cover the span of the control period. The upper respiratory infections category included such items as coryzas, pharyngitis, tonsillitis, bronchitis, and middle ear infections. The gastrointestinal disturbances group was composed of the fever, vomiting, and diarrhea complex. The common communicable diseases were mostly chickenpox and mumps. The miscellaneous group was heterogeneous, containing entries as diverse as trauma and the allergies.

Table 3 was constructed before the real identities of the placebo-control and the virus-fed groups were known. It cannot, therefore, be used to compare the illnesses in the two groups. However, it does serve to show the pattern of illness in the village through the control period. That there was a pattern is self-evident: The predominant type of illness in February between the first two feedings was of the upper respiratory infection type. The predominant illness between the second and third feedings late in February and through the month of March was the gastrointestinal disturbance. Remarkably enough, the percentage occurrences of these two types of illness through both the designated time intervals are almost precisely interchangeable.

The two sections of table 4, one for adults and one for children, were constructed after the identities of the group A and group B participants became known. The table is arranged so that it is possible to compare the illnesses in the placebo-control group with the illnesses in the virus-fed group week by week through the control period. For this table the diagnosed communicable diseases were dropped from consideration, as were other illnesses and complaints that were grossly remote from being considered as a possible "reaction." The upper respiratory infection and gastrointestinal disturbance categories remain in the table. Fever alone, without any other symptoms or signs, has been added. The category "other" includes such symptoms as might possibly be due to the effect of virus on the central nervous system.

TABLE 4.—*Occurrence of Symptoms, by Clinical Type and by Experimental Group, During the Control Period*[*]

	Respiratory		Gastro-intestinal (Diarrhea)		Fever Alone		Other	
Period	Virus	Placebo	Virus	Placebo	Virus	Placebo	Virus[†]	Placebo[‡]
			CHILDREN[§]					
2/3[‖] -2/8	2	4	2	2		2		
2/9 -2/15	10	10	2	2			1	1
2/16 -2/23	8	4	4	1		3		
2/24[‖]-3/1	14	14	6	7	1	2		
3/2 -3/8	3		5	3		1	1	
3/9 -3/16	2	2	8	7				
3/17[‖]-3/22	5	3	19	12			1	
3/23 -3/31	1	2	4	3	1			
Totals	45	39	50	37	2	8	3	1
			ADULTS[¶]					
2/3[‖] -2/8	1	4	4	2				1[#]
2/9 -2/15	14	15	3	2		1		
2/16 -2/23	5	4	7					
2/24[‖]-3/1	6	6	12	6	1			
3/2 -3/8	4	2	7	1				
3/9 -3/16	1	3	9	19				
3/17[‖]-3/22	2	1	33	33				2[**]
3/23 -3/31		3	12	6				
Totals	33	38	87	69	1	1		3

[*] 1st half of study.

[†] 1 complaint of dizziness, 1 of headache, and 1 of soreness in neck region.

[‡] Red "blotches" on body.

[§] Total in virus group, 132; total in placebo group, 125. Total symptoms of all kinds in virus group, 100/132 (75.8%); total symptoms of all kinds in placebo group, 85/125 (68.0%).

[‖] Denotes feeding dates.

[¶] Total in virus group, 147; total in placebo group, 142. Total symptoms of all kinds in virus group, 121/147 (82.3%); total symptoms of all kinds in placebo group, 111/142 (78.2%).

[#] Headache, dizziness, stiff neck (?).

[**] Headache.

There was, of course, some variation in the relative frequency with which symptoms or illnesses occurred week by week in the two participating groups. But for those weeks when the reported incidence for any type of illness was at its peak, the comparative frequency was very close if not identical. For example, in adults, note the comparative frequency of reports of upper respiratory disease for the week of Feb. 9 and the comparative frequency of gastrointestinal disturbance for the week of March 17. Similarly, in children, note the incidences of upper respiratory disease for the weeks of Feb. 9 and 24 and the incidences of gastrointestinal disturbances from Feb. 24 on. There were only two adults with fever as the sole symptom, one in the placebo-control group and one in the virus-fed group. Among children there were 10 such recordings, with the placebo-control group showing 8 and the virus-fed group 2 of them. The three adults who showed "other" symptoms were all in the placebo-control group. The two with headaches alone admitted that they frequently suffered from this complaint. The symptoms of headache, dizziness, and questionable stiff neck in the third adult appeared within 24 hours of feeding and disappeared overnight. Among the virus-fed children there was one complaint of dizziness, one of headache, and one of soreness in the neck. None of these symptoms persisted. One of the placebo-control children developed red "blotches" on the body. The exact nature of this rash was not determined.

TABLE 5.—*Composition of Mediums and Diluent*

Lactalbumin Hydrolysate–Yeast Extract (LHYE)	
Lactalbumin hydrolysate	5.0 gm.
Glucose	4.5 gm.
Yeast extract	1.0 gm.
1% Phenol red	1.6 ml.
Earle's balanced salt solution	1 liter
Growth Medium	
LHYE	80.0 ml.
Human serum	20.0 ml.
5% Sodium bicarbonate	2.0 ml.
Penicillin	100 units/ml.
Streptomycin	100 mcg./ml.
Maintenance Medium	
LHYE	95.0 ml.
Poliomyelitis antibody-free calf serum	2.0 ml.
5% Sodium bicarbonate	2.0 ml.
Penicillin	100 units/ml.
Streptomycin	100 mcg./ml.
Diluent	
Hank's balanced salt solution	85.0 ml.
2% Yeast extract	5.0 ml.
1.4% Sodium bicarbonate	5.0 ml.
10% Glucose	2.5 ml.
Penicillin	100 units/ml.
Streptomycin	100 mcg./ml.

It appears, therefore, that over all there was no overwhelming preponderance of symptoms or symptom constellations limited to one or the other of the experimental groups. The differences in the total occurrence of symptoms of all kinds noted below the body of table 4 are not statistically significant for either adults or children. There is no reason, therefore, to believe that the virus was responsible for any type of symptom or any type of reaction pattern.

In addition, it is interesting to note that the pattern of illness shown in tables 3 and 4 was exactly the pattern of illness that was occurring in the city outside the village limits. The participants themselves observed that the nonparticipants in the village were coming down with exactly similar illnesses. Certainly it is no surprise to note a good deal of respiratory infection in February and March. The gastrointestinal disturbance was occurring not only in the village but also in the city at large, and indeed over the entire state. Reports of diarrhea epidemics were coming in to the state health department from communities more than 100 and often 200 miles away from Minneapolis and from all corners of the state.

Members of the project team examined seven families in whom this gastrointestinal disturbance was occurring. Four of these were in the A group and three in the B group, although at the time the examiners did not know which group was virus-fed. They found the disease to be a definite clinical entity similar in nature in all the families examined regardless of group designation.

Laboratory Methods

Preparation of Tissue-Culture Tubes for Antibody Titrations.—HeLa cells were grown in milk dilution bottles which were seeded with 10^6 cells in 10 ml. of growth medium (table 5) and incubated at 37 C for two days, after which 2 ml. of human serum was added. A replacement feeding of 5 ml. of growth medium was made on the fourth and sixth days of incubation. If cell growth had not followed the expected pattern the feeding schedule was varied. After a total of seven days of incubation, cells were removed from the bottle surface by trypsinization or scraping with a rubber "policeman." Cells from 7 to 10 bottles were pooled and a cell count made in a hemacytometer. The cell suspension was diluted in growth medium to contain 10^5 cells per millimeter and dispensed in 0.5-ml. quantities into 5-in. tissue-culture tubes. The tubes were tightly stoppered with rubber stoppers and incubated in a stationary position in Seelye racks for three or four days. Growth medium was removed and the cell sheets in the tubes were rinsed three times with 1.0 ml. of Hank's balanced salt solution to remove all trace of human serum. Maintenance medium (0.9 ml.) (table 5) was dispensed into each tube.

Poliovirus Pools.—Poliovirus pools were prepared with unmodified strains in quantities sufficient to use through the entire study. Growth medium was removed from HeLa cell bottle cultures which had a population of approximately 10^7 cells per bottle. Cell sheets were rinsed three times with 10 ml. of Hank's balanced salt solution, after which 10 ml. of maintenance medium was added. Bottles were inoculated with 1 ml. of poliovirus type 1 (Mahoney), type 2 (MEF-1), or type 3 (Saukett) diluted 10^{-1}. Bottles incubated at 37 C were observed microscopically daily for cytopathogenicity. When 75 to 100% of the cells were destroyed the bottles were placed at -20 C. Pools of each type were made and were centrifuged (10 minutes, 2,000 rpm no. 2 horizontal) to remove cell debris. Each pool was dispensed into all-glass ampuls (0.3-0.5 ml. per ampul), sealed, and stored at -70 C. Titrations on each pool were carried out in half-log dilutions to determine the 50% tissue-culture infective dose ($TCID_{50}$). Two or three ampuls for each type pool were titrated. The $TCID_{50}$ was calculated by the method of Reed and Muench.

Serum Specimens.—Serum specimens were stored at -20 C. Specimens collected prior to all vaccine and placebo feeding and those collected at the end of the control period (when group B had received vaccine and group A had not) were held until the collection of the third blood specimens, three weeks after the entire group had been fed, at which time all three specimens from each individual were tested in the same test run.

Neutralizing Antibody Test Procedure.—Five fourfold serial dilutions (1:4 through 1:1,024) of each serum specimen were prepared and dispensed in 0.15-ml. amounts into three rows of tubes. Each type of virus pool diluted to contain 100 $TCID_{50}$ per 0.1 ml. was added to one row of serum dilution tubes in 0.15-ml. amounts. Each serum-virus mixture (0.2 ml.) was inoculated into one tissue-culture tube after standing one hour at room temperature. Inoculated tubes were incubated at 37 C for four days.

Controls.—A control serum specimen previously titrated and known to contain neutralizing antibodies for each type of poliovirus was retitrated in each test run. Also with each test run tissue-culture tubes were inoculated with each type of virus pool diluted to contain 100, 10, and 1 $TCID_{50}$ to determine the precise quantity of virus used. An antibody run was not considered satisfactory unless the control virus titration showed the presence of at least 30 $TCID_{50}$ of virus. In most antibody runs, 100-300 $TCID_{50}$ of each virus had been present. Serum controls were not used routinely after 118 serum specimens proved to have no toxic effect on cells in a 1:4 dilution.

Reading.—Inoculated tubes were examined microscopically after four days of incubation. Cytopathogenic effect was graded as approximately 25%, 50%, 75%, or 100% cell destruction. The neutralization end-point was expressed as the reciprocal of the highest dilution of serum which completely neutralized the virus test dose.

Results

The results of the antibody titrations are shown in figures 1 and 2 for children and in figures 3 and 4 for adults. These figures combine the correlation square type of presentation with the percentage of positive responses both gross and by sixteenfold or greater rise displayed alongside each square.

In figure 1, which deals with the virus-fed children, it can be seen that for each type the concentration of recorded results in the cells above the square's diagonal indicates that over-all there was a marked tendency toward positive responses. In those who began the study with titers of less than 1:4 there was a change in a positive direction to any titer in 89.7% of the cases for type 1, in 87.5% of the cases for type 2, and in 85.5% of the cases for type 3. Again beginning with those whose titers were less than 1:4 prefeeding and counting only cases with a sixteenfold or a greater rise in titer, it is seen that such a response was elicited in 70.3% for type 1, 76.0% for type 2, and 70.0% for type 3. The positive changes in titer for those who initially had titers of 1:4 or more might be considered "booster" effects. The extents of these at the various titer levels may be appreciated by consulting the figures.

The results for the placebo-control children, as is evident in figure 2, are markedly different. Here, the cells with recorded results tend to hug the square's diagonal and the percentages of positive responses, however measured, are either zero or of low magnitude. The general picture is that of no change in the postfeeding status as compared to the prefeeding status.

Certain of the cells below the diagonals show figures in parentheses. These represent the infant population of that particular cell. At first glance, this might suggest a lack of antigenicity on the part of the vaccine for infants. However, it should be remembered that in infants two forces are at work to determine the antibody level. There is first the declining titer of the antibodies passively acquired by the infant from the mother. Then there is the possible antigenic effect of the vaccine on the infant itself. The resultant might very well be a "holding" action in which the attrition of maternally transmitted antibodies between the time the first and the last blood specimens were drawn (134 days) is masked and in a sense overcome by the introduction of new vaccine-induced antibodies.

It can be noted that there were some in the placebo-control children's group who did show a bettering of titer. In four of these homologous virus was recovered from the stool, indicating immunization by interfamilial spread from the virus-fed group. Most of the other rises in titer in this class of placebo-control children were only fourfold and could be considered within the limits of usual laboratory procedure variability. Still there are four instances left where it is not an improbable conjecture that the immunization was effected by interfamilial spread of virus even though such virus was not recovered from the stool of the beneficiary.

The most that can be said for the analogous data for adults, as shown in figures 3 and 4, is that there appears to be a trend toward positive responses.

	Post-feeding titers Type 1							Positive	Responses
Pre-feeding titers	<4	4	16	64	256	1024	Totals	Gross	16x or >
<4	18	34	58	29	24	12	175	89.7%	70.3%
4	2(1)	3	6	11	8	5	35	85.7%	68.6%
16		1(1)	1	8		6	16	87.5%	37.5%
64		1(1)	2(2)	1	4	5	13	69.2%	38.5%
256			1(1)	1	4	3	9	33.3%	-
1024					1	6	7	-	-
Totals	20	39	68	50	41	37	255		
	Type 2								
Pre-feeding titers	<4	4	16	64	256	1024	Totals		
<4	13	12	27	23	20	9	104	87.5%	76.0%
4	6(5)	8	13	8	9	16	60	76.7%	55.0%
16		3(3)	3	7	8	18	39	84.6%	66.7%
64	1(1)		2(1)	6	7	8	24	62.5%	33.3%
256		1(1)		1	3	12	17	70.6%	-
1024					1	10	11	-	-
Totals	20	24	45	45	48	73	255		
	Type 3								
Pre-feeding titers	<4	4	16	64	256	1024	Totals		
<4	30	32	42	48	38	17	207	85.5%	70.0%
4	1(1)		6	5	5	2	19	94.7%	63.2%
16			1	5	4		10	90.0%	40.0%
64		1	3(1)	2	2		8	25.0%	0.0%
256		1		2	2	2	7	28.6%	-
1024				1		3	4	-	-
Totals	31	34	52	63	51	24	255		

Figures in parentheses denote infants.

Fig. 1.—Antibody responses in children, virus-fed.

Post-feeding titers

Type 1

Pre-feeding titers	< 4	4	16	64	256	1024	Totals	Positive Gross	Responses 16x or >
< 4	80	2(1*)	1	1	1*		85	5.9%	3.5%
4	11	5	2				18	11.1%	0.0%
16		2	5	1			8	12.5%	0.0%
64		1		2	1		4	25.0%	0.0%
256				3		1	4	25.0%	-
1024						3	3	-	-
Totals	91	10	8	7	2	4	122		

Type 2

Pre-feeding titers	< 4	4	16	64	256	1024	Totals		
< 4	44	6(1*)	1		1*		52	15.4%	3.8%
4	14	11	1				26	3.8%	0.0%
16	1	6	11	3	1		22	18.2%	4.5%
64			4	8			12	0.0%	0.0%
256			1	2	3	1	7	14.3%	-
1024					2	1	3	-	-
Totals	59	23	18	13	7	2	122		

Type 3

Pre-feeding titers	< 4	4	16	64	256	1024	Totals		
< 4	103	3		1			107	3.7%	0.9%
4	6						6	0.0%	0.0%
16	1	1	2				4	0.0%	0.0%
64		1					1	0.0%	0.0%
256			1		1		2	0.0%	-
1024					2		2	-	-
Totals	110	5	3	1	3	0	122		

Figures in parentheses denote infants.
*Denotes virus isolation.

Fig. 2.—Antibody responses in children, placebo-control.

Post-feeding titers

Type 1

Pre-feeding titers	<4	4	16	64	256	1024	Totals	Positive Gross	Responses 16x or >
<4	18	34	58	29	24	12	175	89.7%	70.3%
4	2(1)	3	6	11	8	5	35	85.7%	68.6%
16		1(1)	1	8		6	16	87.5%	37.5%
64		1(1)	2(2)	1	4	5	13	69.2%	38.5%
256			1(1)	1	4	3	9	33.3%	-
1024					1	6	7	-	-
Totals	20	39	68	50	41	37	255		

Type 2

Pre-feeding titers	<4	4	16	64	256	1024	Totals	Positive Gross	Responses 16x or >
<4	13	12	27	23	20	9	104	87.5%	76.0%
4	6(5)	8	13	8	9	16	60	76.7%	55.0%
16		3(3)	3	7	8	18	39	84.6%	66.7%
64	1(1)		2(1)	6	7	8	24	62.5%	33.3%
256		1(1)		1	3	12	17	70.6%	-
1024					1	10	11	-	-
Totals	20	24	45	45	48	73	255		

Type 3

Pre-feeding titers	<4	4	16	64	256	1024	Totals	Positive Gross	Responses 16x or >
<4	30	32	42	48	38	17	207	85.5%	70.0%
4	1(1)		6	5	5	2	19	94.7%	63.2%
16			1	5	4		10	90.0%	40.0%
64		1	3(1)	2	2		8	25.0%	0.0%
256		1		2	2	2	7	28.6%	-
1024				1		3	4	-	-
Totals	31	34	52	63	51	24	255		

Figures in parentheses denote infants.

Fig. 1.—Antibody responses in children, virus-fed.

Post-feeding titers

Type 1

Pre-feeding titers	< 4	4	16	64	256	1024	Totals	Positive Gross	Responses 16x or >
< 4	80	2(1)*	1	1	1*		85	5.9%	3.5%
4	11	5	2				18	11.1%	0.0%
16		2	5	1			8	12.5%	0.0%
64		1		2	1		4	25.0%	0.0%
256				3		1	4	25.0%	-
1024						3	3	-	-
Totals	91	10	8	7	2	4	122		

Type 2

Pre-feeding titers	< 4	4	16	64	256	1024	Totals	Positive Gross	Responses 16x or >
< 4	44	6(1)*	1		1*		52	15.4%	3.8%
4	14	11	1				26	3.8%	0.0%
16	1	6	11	3	1		22	18.2%	4.5%
64			4	8			12	0.0%	0.0%
256			1	2	3	1	7	14.3%	-
1024					2	1	3	-	-
Totals	59	23	18	13	7	2	122		

Type 3

Pre-feeding titers	< 4	4	16	64	256	1024	Totals	Positive Gross	Responses 16x or >
< 4	103	3		1			107	3.7%	0.9%
4	6						6	0.0%	0.0%
16	1	1	2				4	0.0%	0.0%
64		1					1	0.0%	0.0%
256			1		1		2	0.0%	-
1024					2		2	-	-
Totals	110	5	3	1	3	0	122		

Figures in parentheses denote infants.
*Denotes virus isolation.

Fig. 2.—Antibody responses in children, placebo-control.

Post-feeding titers

Type 1

Pre-feeding titers	< 4	4	16	64	256	1024	Totals	Positive Gross	Responses 16x or >
< 4	39	20	7	3		1	70	44.3%	15.7%
4	4	12	14	4	1		35	54.3%	14.3%
16		8	21	16	5		50	42.0%	10.0%
64		2	9	24	19	3	57	38.6%	5.3%
256			3	13	18	13	47	27.7%	-
1024				2	12	9	23	-	-
Totals	43	42	54	62	55	26	282		

Type 2

Pre-feeding titers	< 4	4	16	64	256	1024	Totals	Positive Gross	Responses 16x or >
< 4	26	19	10	1	1		57	54.4%	21.1%
4	2	13	5	8	2		30	50.0%	33.3%
16	1	8	21	11	11	3	55	45.5%	25.5%
64		3	14	15	14	8	54	40.7%	14.8%
256	1		3	13	22	11	50	22.0%	-
1024				4	14	18	36	-	-
Totals	30	43	53	52	64	40	282		

Type 3

Pre-feeding titers	< 4	4	16	64	256	1024	Totals	Positive Gross	Responses 16x or >
< 4	68	21	16	6	3		114	40.4%	21.9%
4	6	10	11	4	1		32	50.0%	15.6%
16		10	14	7	4		35	31.4%	11.4%
64		1	12	24	11	5	53	30.2%	9.4%
256			2	10	13	9	34	26.5%	-
1024				1	6	6	13	-	-
Totals	74	42	55	52	38	20	281		

Fig. 3.—Antibody responses in adults, virus-fed.

Post-feeding titers

Type 1

Pre-feeding titers	<4	4	16	64	256	1024	Totals	Positive	Responses
								Gross	16x or >
<4	32	4					36	11.1%	0.0%
4	1	9	5	1			16	37.5%	6.3%
16	1	5	13	5	2		26	26.9%	7.7%
64		1	5	14	5		25	20.0%	0.0%
256			1	4	10	7	22	31.8%	-
1024				2	5	5	12	-	-
Totals	34	19	24	26	22	12	137		

Type 2

Pre-feeding titers	<4	4	16	64	256	1024	Totals	Positive Gross	Responses 16x or >
<4	23	4	1				28	17.9%	3.6%
4	1	5	1		1		8	25.0%	12.5%
16		6	8$_1$*	12	1		27	48.1%	3.7%
64		1	8	8$_1$*	11	1	29	41.4%	3.4%
256			1	8	14	3	26	11.5%	-
1024			2	2	5	9	18	-	-
Totals	24	16	21	30	32	13	136		

Type 3

Pre-feeding titers	<4	4	16	64	256	1024	Totals	Positive Gross	Responses 16x or >
<4	54	7					61	11.5%	0.0%
4	7	6	2	2			17	23.5%	11.8%
16	1	3	10	2			16	12.5%	0.0%
64		1	4	11	6	2	24	33.3%	8.3%
256		1		6	4	4	15	26.7%	-
1024						3	3	-	-
Totals	62	18	16	21	10	9	136		

*Denotes Virus isolation.

Fig. 4.—Antibody responses in adults, placebo-control.

This trend is modest, but it is there. Type 2 virus was recovered from two persons in the placebo-control adult group, but there was no effect noted on the base-line antibody titer in these persons.

The data presented so far represent the results obtained irrespective of prior experience with the Salk vaccine. Even though the findings are available for each poliovirus type classified into the ultimate categories of fathers, mothers, children, and infants, each on the basis of prior Salk vaccine inoculations, no attempt will be made here to draw an analysis so fine. It can be appreciated that some of these ultimate categories turn out to be ridiculously small.

Virus isolation procedures have now been completed on all stool specimens collected during the course of the study. Future publications will use the results obtained to consider the problem of interfamilial spread of the fed virus. Likewise, the effect of the recovered virus on monkeys will be reported.

Comment

The orally administered attenuated polioviruses used as vaccine in this study are clearly effective antigens for children. This effectiveness obviously extends to all three types. When measured by a crude bettering of an original antibody titer of less than 1:4, these viruses were effective in inducing such a change in 85 to 90% of the participants. When measured by the stricter and, from the laboratory standpoint, the more significant criterion of at least a sixteenfold rise in titer, the effectiveness was still apparent in approximately 70% of the participants.

The vaccine was less effective in adults. True enough, a trend is suggested in that the virus-fed group always had better conversion rates than did the placebo-control group. When the upward trend of antibody titers in adults is measured for statistical significance on the basis of sixteenfold increments, the differences in response between the placebo-control group and the virus-fed group are actually found to be statistically significant for all three types. While these differences are not so great as those that occur in the case of children, they are not accidental.

Attenuated viruses used in this study act like naturally occurring viruses in every respect save one. They do not produce clinical disease. They do set up an intestinal infection, as is evidenced by the recovery of virus from the stool after an appropriate interval. They do stimulate the production of circulating antibodies, as is evidenced by the antibody titrations. Other data, available but not shown here, appear to demonstrate two other interesting and important phenomena. First, naturally occurring antibodies prevent the establishment of an intestinal infection by the attenuated viruses; serum antibodies similar to those induced by Salk vaccination do not prevent such an infection. Second, the attenuated viruses appear to effect an anamnestic reaction in those who, at the moment, show no serologic evidence of having been successfully stimulated by the previous use of the formalinized vaccine.

Definitive results were demonstrated in this study in spite of the fact that a substantial portion of the participants had received Salk vaccine. This is important, since it indicates that the presence of a Salk-vaccinated population should not deter further studies of this nature in the United States. It is interesting that, of 140 children who entered the study with a history of three Salk vaccine inoculations, 57% had titers of less than 1:4 to type 1 poliovirus, 20% had the same lack of antibody titers to type 2 poliovirus, and 77% had titers of less than 1:4 to type 3 poliovirus.

There is no good reason now to doubt that the administration of these living strains of poliovirus is a safe procedure. Safety can be implied on the basis of testing in laboratory animals, and this is the method that must of necessity be used when starting with any attenuated strain *de novo*. The greatest confidence in the safety of these strains, however, comes with the knowledge that up to the present over a million doses of these viruses, including all types in completed or uncompleted sequences, have been consumed without report of any confirmed adverse effect.

The question of a return to virulence is always being raised. Specifically, it is asked, will passage through the human intestine, once or serially, increase the neurotropism of these strains to the point of an actual return to virulence for humans? Some evidence exists to show that there is an increased neurotropism after one passage through the human intestine, especially for type 1, when compared to the neurotropic activity of the original virus used as vaccine. There is also evidence that this neurotropism does not increase after a second passage; in fact, it appears to diminish.[11] This failure of neurotropism to persist after serial passages has been noted for attenuated strains other than those used in this study.[12] Sabin [12] has shown that some strains of virus shown to be neurotropic for monkeys by intraspinal injection are not neurotropic for chimpanzees. He suggests that strains of this character could be safely fed to humans. We feel that the occasional demonstration of neurotropism in monkeys after intracerebral or intraspinal injection of relatively large amounts of virus does not by itself constitute sufficient contraindication to the use of these strains in humans. Study of the neurotropic activity of the strains recovered from stool specimens submitted during the course of this project will be reported in detail later.

We realize that there are some unsolved problems on our hands. The lack of responsiveness in adults is troublesome. It has been suggested that this may be a matter of dosage. It has also been suggested that gastric acidity may be an important factor, since there is so marked a difference between the gastric acidities of adults and children. Studies in both of these areas are now being made. Also under trial is the feasibility of immunizing against all three types of poliomyelitis simultaneously with a single feeding of a trivalent preparation. The durability of the antibodies induced by the use of this vaccine is not yet known. It is hoped, with good reason, that they will be durable. This is a question that time and follow-up alone can answer.

Further, we feel that the true effectiveness of an attenuated poliovirus vaccine as well as any other type of vaccine can be gauged only by its behavior in the face of an actual challenge by the disease itself. Ideally, the quickest way to decide this question would be by a placebo-controlled study in an area where the natural incidence of poliomyelitis would be great enough to yield sufficient cases for statistical analysis. Better yet would be such a study during an epidemic situation. These strains have been used twice in association with epidemics of poliomyelitis: once in a type 1 outbreak in Colombia[6] and again in a type 2 outbreak in Nicaragua.[13] However, there were no control populations and the administration of the vaccine in each case was begun after the epidemic peak.

The immunological advantages of a vaccine consisting of living attenuated poliovirus have been mentioned. The economic and administrative advantages are of equivalent importance. The simpler manufacturing process, the lesser costs involved, the ease of oral administration, the ability to eliminate the need for syringes and needles all make such a product ideal for use in those areas of the world where funds, medical equipment, and medical personnel are at a premium.

The results of this study are sufficiently encouraging to lead to the hope that the replacement of virulent polioviruses by attenuated polioviruses will effect the same degree of eradication for poliomyelitis as has been achieved for smallpox by replacing the variola virus with the vaccinia virus.

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ACCURATE DOSAGES FOR NARCOTICS.—Errors can occur in the conversion of doses from the apothecary to the metric system. The routine use of the official (since 1943) metric system should eliminate the problems caused by the troublesome arithmetic of dividing fractions. In preparing the small doses of opiates appropriate for infants and children, it is well that instruction be given in the proper method of dilution of the larger size tablets so that the proper dose can be given in an accurately measurable volume of ½ to 1 cc. All possible care should be taken in the ordering of narcotics to make the orders clear to those who will be administering these potent agents. When patients show signs of undue degrees of depression from normal doses of drugs, or when accidental overdosage . . . produces severe depression of respiration or circulation, then the use of the opiate antagonists will be of great assistance in treating this complication.—Betty J. Bamforth, M.D., Accidental Overdosage of Morphine Used as Preanesthetic Medication, *Wisconsin Medical Journal,* April, 1959.

COMMUNITYWIDE VACCINATION PROGRAM WITH ATTENUATED POLIOVIRUS IN ANDES, COLOMBIA

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An outbreak of paralytic poliomyelitis occurred in southern Antioquia, Colombia, in January, 1958. A census located 2,922 families who agreed to participate in a program of vaccination, and the immune status of the population was ascertained by systematic blood sampling. Oral vaccination with attenuated strains of poliovirus (types 1, 2, and 3) began in May, 1958. Comparison of prevaccination and postvaccination serums showed that, of the vaccinated children who lacked demonstrable antibody at the time of vaccination, 91% responded to type 1 virus, 72% to type 2, and 87% to type 3. Both the safety and the immunizing efficacy of the three strains of virus employed were convincingly demonstrated.

In Colombia paralytic poliomyelitis has been regarded generally as a sporadic disease of minor public health importance. The number of cases reported annually from 1947 to 1957 [1] ranged from 29 to 169, with the highest rate being 1.6 cases per 100,000 population, in 1953.

In contrast to the fact that the paralytic form of the disease is rarely seen, it was shown to be almost universal in parts of the country that children had had poliovirus infection by the age of 2 years.[2] Surveys of the distribution of naturally occurring poliovirus antibodies in Cali and Bogotá indicated that all children 2 years of age or older had antibodies to one or more types of poliovirus, and that in the 7-to-9-year-old group 88% already had antibodies to all three known types. Comparable results have been reported in studies of other areas of the world with similar socioeconomic and hygienic conditions.[3]

Early in January, 1958, the Health Center of Andes, a *municipio* (county) in southern Antioquia, Colombia, with a population of 50,000, began to report cases of paralytic poliomyelitis. By March, nine cases and three deaths had been recorded. Alerted by these reports to the possibility of an incipient epidemic, the health authorities of the *departmento* (state) of Antioquia and the Ministry of Public Health of Colombia requested the Pan American Sanitary Bureau (PASB) to cooperate in a vaccination program making use of the inactivated poliovirus vaccine.

In conformity with the request, one of us (M. M. S.) visited Andes on March 19 to evaluate the situation and assist in identifying the type of poliovirus involved in the outbreak. Stool and blood samples were collected from six persons with paralytic disease and all members of their households. Within a week of collection of the samples, type 1 poliovirus had been isolated from the stools of two persons with the disease and four contacts, and this information was sent to the health authorities in Colombia.

Because the formalinized vaccine is incapable of halting the spread of poliovirus in a community [4] and therefore could not be expected to alter the course of an epidemic, and since it seemed likely that an outbreak was in progress, a plan was developed to vaccinate children of the more highly susceptible age groups in Andes with orally administered live attenuated poliovirus vaccine. The plan was formulated on the basis of previous experience with the vaccine in Minnesota [5] and of suggestions of the Expert Committee on Poliomyelitis of the World Health Organization [4b] regarding the field uses of live poliovirus vaccines "in the face of an impending epidemic." Additional reasons for advocating this type of vaccine were (*a*) the relative simplicity of oral administration of vaccine; (*b*) the long-lasting protection apparently conferred by the vaccine, as measured by circulating antibodies,[5A] making less frequent, or perhaps even unnecessary, the need for booster doses; and (*c*) its capacity to induce within the alimentary tract a high degree of resistance to the virus, thus offering the possibility of reducing and eventually eliminating the spread of virulent paralytic strains of poliovirus from the community.

Geographical and Population Data

The *municipio* of Andes is situated at the southwestern tip of Antioquia and covers an area of approximately 241 square miles of extremely mountainous terrain with altitudes ranging from 3,300 to 11,500 ft. The principal community, the town of

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State Health Officer Antioquia, Colombia (Dr. Abad-Gómez), State Health Department, Antioquia, Colombia (Dr. Piedrahita), Department of Preventive Medicine and Public Health, School of Medicine, Medellin-Antioquia, Colombia (Dr. Solórzano), and Pan American Sanitary Bureau, World Health Organization (Dr. Martins da Silva).

Andes, is connected by an unsurfaced road with Medellín, the capital of the state, 83 miles to the north.

Andes is a typical rural, agricultural county, with coffee as the principal cash crop. As in many South American coffee-growing areas, the production of essential foodstuffs is negligible and dietary deficiencies and malnutrition are widespread.

The county contains 20 population groupings, 8 of which can be reached by automobile and 12 only by mule trail. Of the estimated population of 50,000, approximately 7,000 live in the town of Andes and the remainder in rural areas. In the urban area, 54% of the dwellings have bathing facilities, 74% have latrines or privies, and 91% have water available on the premises. In rural areas, housing is universally poor, lacking running water and sanitary privies.

The median family consists of seven members. In the study area the distribution of the population by age group is 37% under 7 years, 11% between 7 and 10 years, and 52% over 10 years, as determined by the census made as a part of this study. The reported morbidity from typhoid was 425 per 100,000 in 1957 (Antioquia Health Department Reports).

TABLE 1.—*Distribution of Naturally Occurring Poliovirus Antibodies Among Children, Andes, Colombia, 1958*

Age Group, Yr.	No. of Serums or of Children	% of Serums with Antibodies to Poliovirus							% Without Antibody to Types 1, 2, or 3
		3 Types—1, 2, and 3	2 Types			1 Type Only			
			1 and 2	1 and 3	2 and 3	1	2	3	
6-11 mo.	40	5.0	10.0	7.5	7.5	22.5	10.0	2.5	35.0
1	43	...	11.6	2.3	...	32.6	...	4.7	48.8
2	68	26.5	7.4	5.9	8.8	14.7	11.8	2.9	22.0
3	82	36.6	13.4	9.8	7.3	13.4	7.3	4.9	7.3
4	91	52.7	14.3	6.6	9.9	4.4	3.3	4.4	4.4
5-6	180	66.7	12.2	2.2	6.7	5.6	0.5	3.3	2.8
7-9	125	84.0	5.6	1.6	6.4	0.8	...	...	1.6
10 and over*	61	90.2	6.6	1.6	...	...	1.6	...	...
Total	690	54.8 (378)†	10.3 (71)	4.2 (29)	6.4 (44)	8.5 (59)	3.3 (23)	2.8 (19)	9.7 (67)

* Includes a small number of adults.
† Figures in parentheses indicate total number of serums or persons in each category.

Material and Methods

A project headquarters was set up in the town of Andes with a full-time staff of three physicians (including two epidemiologists: the project director and the PASB project consultant) and one graduate and six auxiliary nurses. Other personnel included a laboratory technician, a health educator, an observer-virologist from the laboratory that produced the vaccine, and the PASB regional adviser on poliomyelitis. Cooperation of community leaders, particularly those of the church, was enlisted through careful explanation of the objectives of the program and the details of the plan of operation.

Vaccination was started on May 5, 1958. In the town of Andes, vaccination was carried out on a house-to-house basis. Elsewhere, the inhabitants of each area gathered at one of the 19 vaccination points, usually a school or church. Five of these vaccination centers were beyond the limits of the county of Andes, in areas where cases of paralytic poliomyelitis had developed.

Vaccination was limited to children between the ages of 2 months and 6 years inclusive. Children under 7 years of age had been shown to be, serologically, the group most susceptible to the disease.[2] Furthermore, all cases of paralytic poliomyelitis in the present Andes outbreak occurred in children under 6 years of age. In view of the high infant mortality in the area, particularly in the first 2 months of life, infants under 2 months of age were excluded to avoid association of vaccination with illness or death due to unrelated causes. The consensus was that these babies would be subjected to no unusual risk, since they would be protected by maternal poliovirus antibodies.[6]

For field trial purposes, the county was divided into 16 sections. Before vaccination, a census was taken of all families that agreed to have their children vaccinated. Blood samples were taken from the children to be vaccinated and from their siblings aged 7 to 9 years inclusive. The latter group served as contacts in whom evidence of virus spread might be sought in the postvaccination period.

A record was kept of the following information for each child vaccinated and each contact bled: name of each subject, age, sex, parents' names, address, dates of vaccination and bleeding, and postvaccination clinical observations. The epidemiologic follow-up and bleeding of vaccinated children and their contacts was conducted in collaboration with the Health Center of Andes and with the assistance of the seven physicians who practice in the area.

At the time of first vaccination parents were instructed that in the event of any illness in the family after the administration of the vaccine they should apply for medical advice and assistance either to the Health Center or to a temporary center especially established for this project. As a result, attendance at the health centers increased greatly and medical surveillance in the area was generally improved. After the feeding of the type 1 vaccine, participants in the program were observed and questioned at intervals of three or four weeks that is, at the times of feeding the type 2 and type 3 vaccines and on collection of the postvaccination blood samples. In the town of Andes, members of the nursing or medical staff of the project made visits every two weeks to the homes of participants from the time of the first feeding of vaccine through the collection of postvaccination blood samples and entered any pertinent medical data on the individual records. Since completion of the vaccination program, observation of all vaccinated and contact children has been continued through the cooperation of the staff of the Health Center, the locally practicing physicians, and alerted community leaders.

TABLE 2.—*Antibody Response of Vaccinated Children, Andes, Colombia, 1958*

	Type 1			Type 2			Type 3		
	Total No. Fed	Positive Responses*		Total No. Fed	Positive Responses*		Total No. Fed	Positive Responses*	
Prefeeding Titers		No.	%		No.	%		No.	%
<1:4	128	116	91	151	108	72	179	156	87
1:4	8	6	75	2	1	50	10	8	80
1:8	16	13	81	29	20	69	47	38	81
1:16	12	8	67	5	1	20	13	11	85
1:32	48	34	71	41	28	68	70	44	63
1:64	16	5	31	8	6	75	17	15	88
1:128	79	44	56	55	34	62	64	32	50
1:256	36	9	25	15	8	53	12	4	33
1:512	68	14	21	56	23	41	32	7	22
1:1,024	11	...	...	12	...	...	2	...	...
>1:1,024	30	...	...	81	...	...	11	...	...
Totals	411†	249	61	362‡	229	63	444§	315	71

* Fourfold or more.

† 41 with titers of 1:1,024 or greater before and after feeding omitted from total

‡ 93 with titers of 1:1,024 or greater before and after feeding omitted from total.

§ 13 with titers of 1:1,024 or greater before and after feeding omitted from total.

TABLE 3.—*Antibody Response of Unvaccinated Contacts, Andes, Colombia, 1958*

	Type 1			Type 2			Type 3		
	Total No. Fed	Positive Responses*		Total No. Fed	Positive Responses*		Total No. Fed	Positive Responses*	
Prefeeding Titers		No.	%		No.	%		No.	%
<1:4	9	6	67	3	2	67	6	1	17
1:4	1	1	100	5	3	60	2	1	50
1:8	4	3	75	3	1	33	15	5	33
1:16	7	4	57	7	5	71	11	4	36
1:32	25	9	36	20	8	40	42	19	45
1:64	10	3	30	10	2	20	6	1	17
1:128	37	10	27	31	12	39	32	11	34
1:256	10	2	20	9	1	11	5	1	20
1:512	21	2	10	20	4	20	11	2	18
1:1,024	2	...	...	7	...	...	1	...	...
>1:1,024	8	...	...	19	...	...	3	...	...
Totals	124†	40	32	108‡	38	35	130§	45	35

* Fourfold or more.

† 10 with titers of 1:1,024 or greater before and after feeding omitted from total.

‡ 26 with titers of 1:1,024 or greater before and after feeding omitted from total.

§ 4 with titers of 1.1,024 or greater before and after feeding omitted from total.

The attenuated strains of poliovirus type 1 (SM strain), type 2 (MEF-1 strain), and type 3 (Fox strain) were used in the vaccine. The passage histories of these strains were identical to those used in the 1958 Minnesota trial.[5b] The vaccine was dispensed in hard gelatin capsules in which the virus was adsorbed on granular gelatin.

The vaccination program was carried out in three steps. Children were fed first one capsule containing $10^{4.9}$ TCID$_{50}$ (50% tissue-culture–infective dose) of type 1 virus (pool 7-1231-115A), the virus type isolated during the Andes outbreak; four weeks later they were given two capsules containing a total of $10^{5.3}$ TCID$_{50}$ of type 2 virus (pool 7-1232-213); and three weeks thereafter they received one capsule containing $10^{5.1}$ TCID$_{50}$ of type 3 virus (pool 7-1232-318). For the feeding of small children, the capsules were opened and the contents were mixed with water and administered by spoon.

In order to ascertain the immune status of the population, prior to the administration of the type 1 poliovirus vaccine, blood samples were collected from 690 individuals, all but 61 of whom were between 6 months and 10 years of age. These specimens were obtained throughout the study area by bleeding the children within this age group in every 10th family among the 2,922 families participating. The data regarding these serums are assembled in table 1.

TABLE 4.—*Distribution of Titers and Mean Titers of Serums Before and After Live Attenuated Poliovirus Vaccination in 428 Children*

			% of Serums with Titers of						Geometric Mean Titer	
			<1:4		1:4 to 1:64		>1:64			
Age, Yr.	No. of Serums or Children	Type of Virus	Pre	Post	Pre	Post	Pre	Post	Pre	Post
<1	36	1	61	6	14	11	25	83	6	267
	36	2	67	36	33	45	0	19	2	8
	36	3	75	17	22	53	3	30	2	29
1	10	1	55	5	0	80	45	87	15	305
	40	2	93	22	7	53	0	25	1	16
	40	3	93	15	5	33	2	52	1	45
2	59	1	44	10	19	20	37	70	15	131
	60	2	42	13	15	27	43	60	25	129
	60	3	57	5	28	52	15	43	5	54
3	70	1	31	1	14	9	55	90	38	291
	71	2	37	8	15	24	48	68	34	195
	70	3	41	1	36	30	23	69	11	186
4	74	1	23	1	31	20	46	79	42	104
	74	2	19	3	19	20	62	77	95	260
	75	3	23	3	40	23	37	74	28	201
5	77	1	16	1	31	22	53	77	56	192
	75	2	19	7	17	14	64	79	112	294
	76	3	26	3	39	27	35	70	22	149
6	68	1	9	2	23	22	68	76	295	200
	69	2	10	1	23	16	67	83	136	338
	69	3	18	4	43	33	39	63	32	173

Five hundred ninety-one of the 690 individuals who were bled initially were rebled one month after the administration of the third dose, i. e., type 3 poliovirus vaccine. The prevaccination and postvaccination blood specimens were titrated in fourfold dilutions to determine the immunologic response of the children to the vaccine and the extent of spread of the vaccine strains to the household contacts.

The paired samples were tested as units of two by the method of Salk, Youngner, and Ward[7] with use of monkey kidney-cell cultures. Each fourfold dilution of serum was tested in duplicate tubes against 100 to 300 TCID$_{50}$ of one or another of the three types of poliovirus. Fifty per cent neutralizing endpoints were calculated by the method of Reed and Muench[8] and the results reported to the nearest twofold dilution. Serologic data thus obtained are summarized in tables 2, 3, and 4. An antibody titer of 1:4 or greater in the postvaccination specimens of children previously lacking demonstrable antibody was considered a positive response. In children with prevaccination antibodies, a fourfold or greater rise in titer was considered a booster response.

Observations and Results

Response to Vaccination.—The numbers of children vaccinated were 7,378 with type 1 virus, 7,122 with types 1 and 2, and 6,977 with all three types. Only 5.5% of the children who started the vaccination schedule did not complete it.

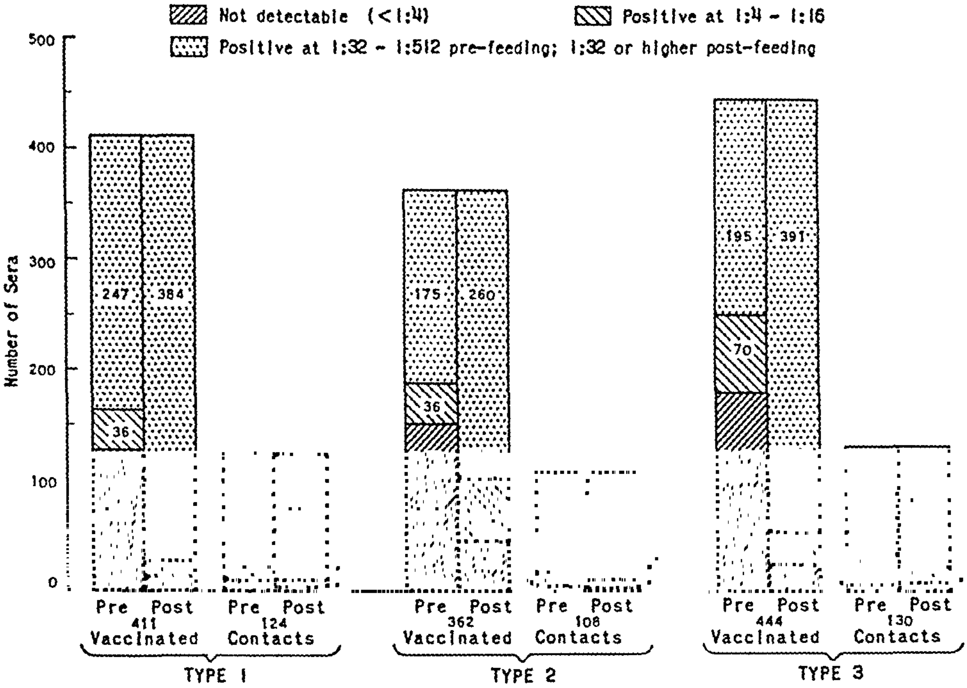

Fig. 1.—Poliovirus antibody response in vaccinated and contact children, before and after feeding of vaccine.

The distribution of naturally occurring poliovirus antibodies in 690 Andes residents prior to vaccination is presented in table 1. Antibodies were not detected for any type of poliovirus in the serums of 9.7% of the children. Antibodies were present for one or two types of virus in the serums of 35.5% and for all three types in 54.8%. Thus 45.2% of the children lacked demonstrable antibody for one or more types of poliovirus.

The poliovirus antibody status of vaccinated children, before and after feeding of vaccine, is summarized in table 2 and figures 1, 2, and 3. It can be seen that a postvaccination conversion from negative to positive occurred in 91% for type 1, 72% for type 2, and 87% for type 3 virus. Booster responses were as follows: in children with prevaccination titers ranging from 1:4 to 1:16, 75% for type 1, 61% for type 2, and 81% for type 3; in children with prevaccination titers ranging from 1:32 to 1:512, 43% for type 1, 57% for type 2, and 52% for type 3.

The antibody status of the household contacts, before and after the vaccination of the index children, is summarized in table 3 and figures 1 and 2. These data show a conversion from negative to positive in six of nine for type 1, two of three for type 2, and one of six for type 3. Relatively lower conversion rates for type 3 might be expected, because the second bleedings took place only one month after the feeding of type 3 vaccine and hence there was less time for contact exposure and for serologic response to that virus strain. In the contacts who showed evidence of natural immunity at the beginning of the vaccine feedings, second samples of serum showed a fourfold or greater booster response as follows: in those with antibody titers originally ranging from 1:4 to 1:16, 67% for type 1, 60% for type 2, and 36% for type 3; in those with an initial range from 1:32 to 1:512, 25% for type 1, 30% for type 2, and 35% for type 3.

The data on prevaccination and postvaccination antibody status of vaccinated and contact children are presented graphically in figures 1 and 2. The serologic data for vaccinated children are summarized by age in table 4, and part of these data are presented graphically in figures 3 and 4. The usual decline in antibody for types 2 and 3 poliovirus among children in the 6-to-11-month age group was not paralleled by the curve for the type 1 antibody. This may reflect the fact that type 1 virus had been prevalent in the community for several months before the collection of the prevaccination specimens. That this higher percentage of children having type 1 antibody is associated with recent infection may be seen in table 4, where the proportion of prevaccination titers of more than 1:64 is far greater for type 1 than for types 2 and 3 among the children under 2 years of age.

A study of individual serologic records revealed that, among the 128 children without demonstrable antibody for type 1 virus before feeding, 6 failed to respond to both type 1 and type 2 vaccine strains and 2 others failed to respond to both type 2 and type 3 vaccines. Of the 151 children lacking type 2 antibody before vaccination, 9 failed to respond to both type 2 and type 3 vaccine strains. Twelve of these children who failed to respond to two of the three vaccine strains lacked antibody for any of the three serologic types of poliovirus prior to vaccination. Failures to respond were most frequent for the type 2 vaccine strain. In addition to those cited above, 27 children, all but 5 of whom were under 4 years of age, failed to respond to type 2 only despite the absence of antibody for this virus type in their prevaccination serums. Sixteen of these 27 children also lacked type 1 antibody at the start of the feeding program.

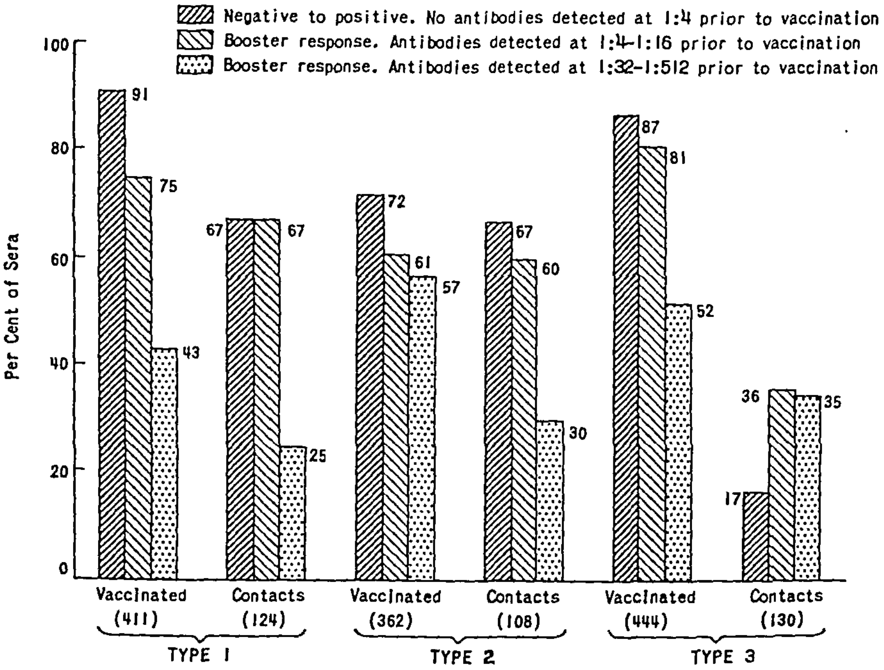

Fig. 2.—Percentage of serums in vaccinated and contact children with a minimum fourfold antibody titer increase after administration of live attenuated poliovirus vaccine.

A survey of the individual vaccination records of those children who failed to respond to vaccination did not reveal significant grouping of failures in time, place, or vaccine consignment. They were randomly distributed over the study area and hence are not suggestive of lack of response resulting from defective or mishandled vaccine or of the localized prevalence of interfering enteric infections, which, presumably, could be found to predominate in the urban segments of the town of Andes.

Epidemiologic Observations.—At the start of the vaccination program, 15 verified cases of poliomyelitis had been reported from the area. After May 5, when the program began, four additional cases were reported, all from sections where the orally given vaccine had not yet been administered. Reported cases occurred in persons ranging in age from 5 months to 6 years, with a median age of 1 year. Up to the time of writing (May, 1959), no cases of poliomyelitis had been recorded among vaccinated children or their contacts.

Vaccinated children showed no untoward reactions. The postvaccination gastrointestinal complaints (such as diarrhea and vomiting) occasionally reported at the health centers or during follow-up visits were no more frequent than would normally be expected in a population highly infested with helminths and intestinal protozoa. In the few instances where symptoms were sufficiently severe to warrant further investigation, stool studies performed at the State Health Laboratory in Medellín frequently revealed parasitic infestation or the presence of pathogenic bacteria.

During the vaccination program (May to August), 17 deaths were recorded among children who had received at least one dose of the vaccine: nine children were less than 1 year of age, and the ages of the others ranged from 1 to 5 years. Diagnoses listed on death certificates by attending physicians were gastroenteritis in nine cases; pneumonia and bronchitis in two cases; and glomerulonephritis, diphtheria, and an overdose of Nivaquina (an antimalarial drug) in one case each. The other three persons were unattended by a physician, but query of the parents revealed that none showed any history suggestive of poliomyelitis or other central nervous system involvement. Seventeen deaths during a period of four months in a population of approximately 7,000 children is less than expected in Andes, where in 1957 the infant mortality was 121 per 1,000 live births and the mortality in the 1-to-4-year age group was approximately 20 per 1,000 population.

Comment

The strains of viruses used in the Andes vaccination program had been extensively tested in various ways in monkeys before their administration to human subjects. While the relationship between virulence for monkeys and pathogenicity for man is difficult to assess, studies of a field strain of type 1 virus that was isolated in Andes prior to the vaccination program from one of the persons with paralysis are interesting. As little as 2 TCID$_{50}$ of this field strain produced complete paralysis when injected intracerebrally in monkeys, whereas 10 million TCID$_{50}$ or more of any of the three attenuated strains used as vaccine rarely induce even slight paralysis when similarly injected.[9]

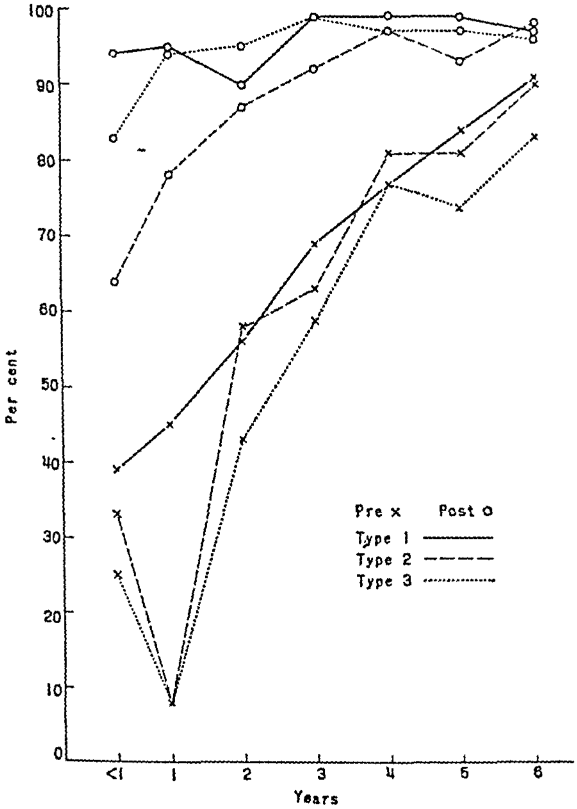

Fig. 3.—Percentage distribution of poliovirus antibodies, by immunotype, before and after vaccination in 428 children, by age.

Laboratory studies in experimental animals are important and essential, but ultimately only field experience on a scale such as that gained in Andes provides an acceptable basis for determining the advisability of the continued use of the viruses employed. The safety of the vaccine strains for human subjects had been ascertained before their use in Andes by small-scale trials in children and adults, totaling about 1,000 persons, of which the most recent are those in Minnesota,[5b] where the behavior of the strains was observed under close supervision in the households of approximately 150 married university students and their children, and in another earlier trial involving 25 infants and their family contacts.[5a]

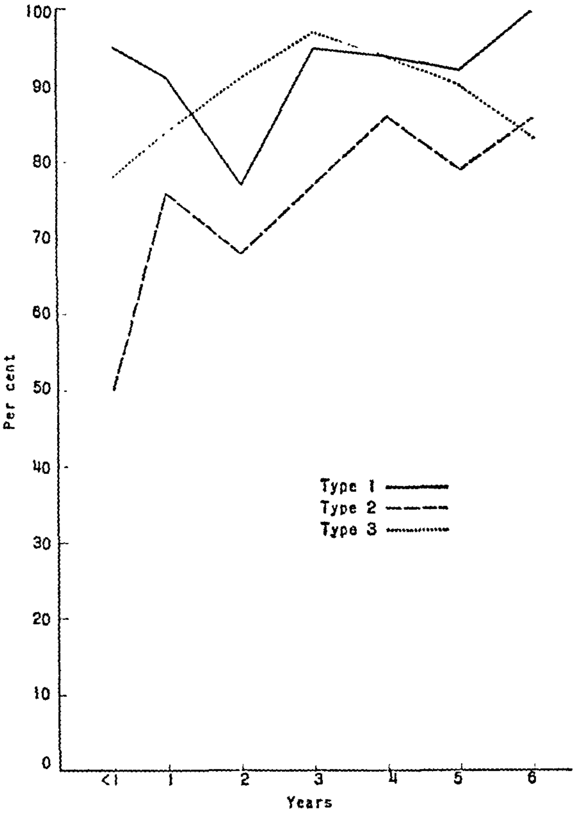

Fig. 4.—Children with type-specific poliovirus antibodies after vaccination as a percentage of those without demonstrable antibodies before vaccination, by age.

The results attained in these studies were the justification for making a larger trial. The data obtained in the present field study confirm the observations made in the former trials and greatly add to the number of susceptible children safely vaccinated.

The prevaccination serologic data summarized in table 1 show that, of the 504 children under 7 years of age, 65 (12.8%) lacked detectable antibody to any of the three types of poliovirus. Most of these fully susceptible children were under 4 years of age. By applying the same percentage of susceptibility to the 7,378 children who received type 1 virus, it can be estimated that 952 children vaccinated with this strain showed triple-negative responses. Similarly, it is estimated that an additional 34 who showed triple-negative responses were are presented graphically in figures 3 and 4. The usual decline in antibody for types 2 and 3 poliovirus among children in the 6-to-11-month age group was not paralleled by the curve for the type 1 antibody. This may reflect the fact that type 1 virus had been prevalent in the community for several months before the collection of the prevaccination specimens. That this higher percentage of children having type 1 antibody is associated with recent infection may be seen in table 4, where the proportion of prevaccination titers of more than 1:64 is far greater for type 1 than for types 2 and 3 among the children under 2 years of age.

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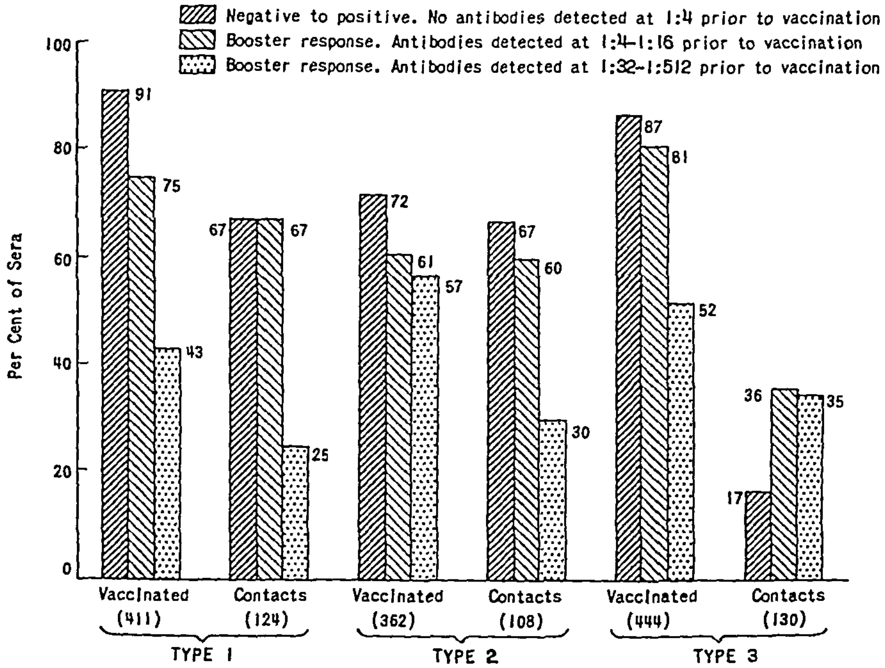

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The strains of viruses used in the Andes vaccination program had been extensively tested in various ways in monkeys before their administration to human subjects. While the relationship between virulence for monkeys and pathogenicity for man is difficult to assess, studies of a field strain of type 1 virus that was isolated in Andes prior to the vaccination program from one of the persons with paralysis are interesting. As little as 2 $TCID_{50}$ of this field strain produced complete paralysis when injected intracerebrally in monkeys, whereas 10 million $TCID_{50}$ or more of any of the three attenuated strains used as vaccine rarely induce even slight paralysis when similarly injected.[9]

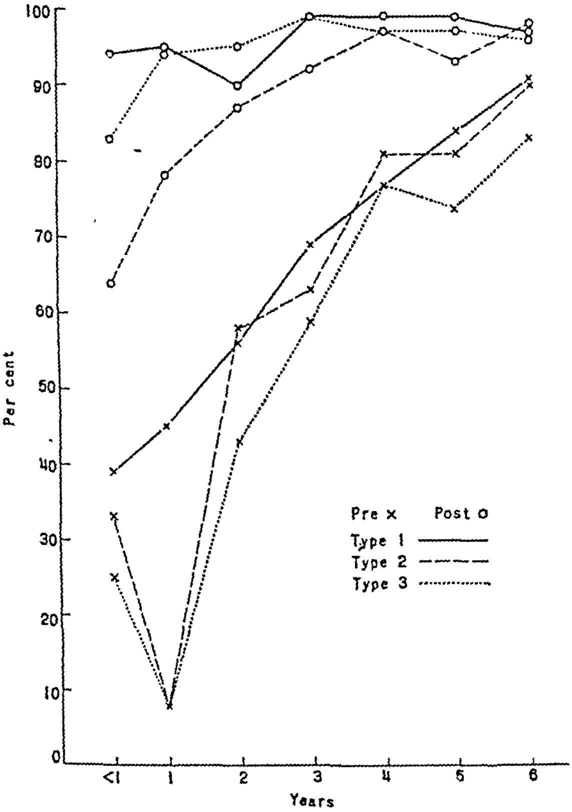

Fig. 3.—Percentage distribution of poliovirus antibodies, by immunotype, before and after vaccination in 428 children, by age.

Laboratory studies in experimental animals are important and essential, but ultimately only field experience on a scale such as that gained in Andes provides an acceptable basis for determining the advisability of the continued use of the viruses employed. The safety of the vaccine strains for human subjects had been ascertained before their use in Andes by small-scale trials in children and adults, totaling about 1,000 persons, of which the most recent are those in Minnesota,[5b] where the behavior of the strains was observed under close supervision in the households of approximately 150 married university students and their children, and in another earlier trial involving 25 infants and their family contacts.[5a]

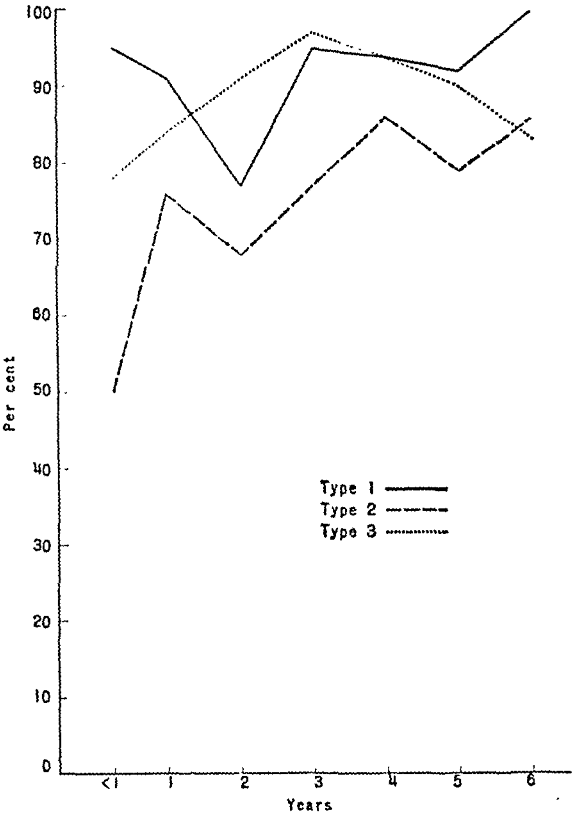

Fig. 4.—Children with type-specific poliovirus antibodies after vaccination as a percentage of those without demonstrable antibodies before vaccination, by age.

The results attained in these studies were the justification for making a larger trial. The data obtained in the present field study confirm the observations made in the former trials and greatly add to the number of susceptible children safely vaccinated.

The prevaccination serologic data summarized in table 1 show that, of the 504 children under 7 years of age, 65 (12.8%) lacked detectable antibody to any of the three types of poliovirus. Most of these fully susceptible children were under 4 years of age. By applying the same percentage of susceptibility to the 7,378 children who received type 1 virus, it can be estimated that 952 children vaccinated with this strain showed triple-negative responses. Similarly, it is estimated that an additional 34 who showed triple-negative responses were among the 2,144 siblings aged 7 to 10 years who were in intimate contact with the vaccinated children, most of whom, it may be assumed, excreted type 1 virus for varying periods of time. Thus an estimated 986 children who showed triple-negative responses after vaccination in the study area are presumed to have been exposed to the type 1 strain of the vaccine.

On the basis of the data summarized in table 2, it may be calculated that 28.3%, or 2,088 children, fed type 1 virus were without homologous antibody protection at the time of feeding. In a like manner, an estimated 33.1%, or 2,357 children, were without antibody to type 2 and 39.1%, or 2,728, were without antibody to type 3 when fed these strains. The high rates of conversion (fig. 4) indicate that vaccination successfully infected a very large proportion of these susceptible children. Among 58 children who originally had triple-negative responses and were rebled after vaccination, 91% responded to type 1, 64% to type 2, and 86% to type 3 poliovirus vaccines. There remained no children with triple-negative responses among those tested after vaccination.

In the absence of any observed indications or signs of central nervous system or other complications in the vaccinated children and their contacts, we believe that continued use of the polioviruses employed in Andes is amply justified.

The circumstances under which the present vaccination program was initiated justified an immediate and direct defense against a type 1 poliovirus epidemic. While it cannot be proved that in the absence of the vaccination program an epidemic would have developed, and no claim is made to have aborted such an epidemic, the measures taken were selected for that purpose. For this reason the type 1 vaccine was fed first, in spite of the fact generally held that the attenuated SM strain of type 1 virus may be sufficiently invasive to "interfere" with subsequent infection by virus of the other two immunotypes.

In the present study, the proportionately greater number of children failing to respond to the type 2 strain suggests that the type 1 strain interfered with the successful establishment of type 2 in the intestines of those lacking antibody to this virus. Also, it may be seen in table 4 that for children under 2 years of age the increment in geometric mean titer for type 1 is much greater than for the other two types. Since it is clear that the relatively lower titers for types 2 and 3 are not due to any inability of children of this age to respond to antigenic stimulation, the recency of their experience with the type 1 vaccine virus may have been a contributing factor in determining their lesser response to the other vaccine strains fed.

In the absence of epidemic threat it appears to be preferable to start an immunizing program with type 2 virus, both because it may have some antigenic overlapping with the other two types of poliovirus [10] and because the type 2 strain used in this study seems to possess a lesser degree of infectivity than either the type 1 or the type 3 strains. The indicated order of feeding would therefore appear to be either types 2, 3, 1; or 2, 1, 3. The data in table 4 for children over 3 years of age show that, in spite of the antigenic overlapping of type 2, antibody for this type, even at relatively high prevaccination levels, did not prevent substantial increments in mean titers for types 1 and 3, nor indeed for type 2 itself.

Summary and Conclusions

In the face of an outbreak of poliomyelitis in Andes, Antioquia, Colombia, an oral vaccination program was carried out on a communitywide basis with attenuated strains of poliovirus representing each of the three virus types. With the participation of local, national, and international health organizations, a staff was assembled to take a census of the area, administer the vaccine, collect prevaccination and postvaccination serum samples from vaccinated and contact children between the ages of 6 months and 9 years, and maintain epidemiologic surveillance of the affected area. Of 7,378 children who began the series of vaccinations, 94.5% completed the three immunizing feedings.

Serologic evidence indicates that, of the vaccinated children who lacked demonstrable type-specific antibody at the time of vaccination, 91% responded to type 1 virus, 72% to type 2, and 87% to type 3. Smaller but significant proportions of those with prior demonstrable antibodies showed fourfold or greater booster responses to vaccination. Of 58 children shown to have negative responses before vaccination to all three types of poliovirus, none remained so after vaccination.

Although four new cases of poliomyelitis were reported in the Andes study area after the start of the oral vaccination program, none of the cases occurred in a vaccinated child or a contact, nor did any of the cases develop in areas where vaccination had begun. Since the start of the vaccination program in May, 1958, there have been no undesirable reactions associated with or attributable to the oral vaccination.

Both the safety and the immunizing efficacy of the strains of virus employed were demonstrated by their performance in an estimated 986 vaccinated or contact children who were without serologic evidence of previous exposure to any type of poliovirus and in between two and three times this number of children who lacked antibody to one or more types of poliovirus.

1501 New Hampshire Ave., N.W. (6) (Dr. Martins da Silva).

The vaccine used in this study was provided by Lederle Laboratories Division, American Cyanamid Company, Pearl River, N. Y., through an agreement with the Pan American Sanitary Bureau.

The specimens were flown under refrigeration to Dr. Herald R. Cox at the Viral and Rickettsial Research Section of Lederle Laboratories. Dr. Cox and staff carried out the virus isolations and antibody titrations reported.

We wish to express our appreciation for the assistance received from the following persons, among many others: Dr. Juan Pablo Llinas, Minister of Public Health of Colombia at the time of the study; Dr. Luis Patiño Camargo, National Director of Health of Colombia; Dr. Vernon B. Link, Chief, Public Health Division, and Miss Anna Obert, Health Education Advisor, U.S.A. Operations Mission to Colombia; and Dr. Anibal Cañas, Director, Health Center of Andes.

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THE ART OF CONSULTATION.—The art of consultation . . . should not be . . . simply a question of sending a patient away for a second opinion; it is the careful selection of the man who, by training and by temperament, is the most suitable for the matter in hand. . . . My partner made it perfectly plain to all his patients that, if they wished, a consultation would immediately be arranged, but also that, if he himself felt the need of a second opinion, no objection should be offered. The patient often requested that a particular individual be summoned, someone perhaps who had operated on another member of the family, or who had given sound advice on a previous occasion; and this request, unless absolutely unsuitable, was invariably granted. In this way, I met many physicians and surgeons from hospitals other than my own, and I learned a great deal from them, but it was my own surgical master, Sir Holburt Waring, who taught me, in a single word, one of the fundamental principles of consultation. Quite recently, I had been his house surgeon, and . . . after ten days [he said], "Really, Abercrombie, you are the worst house surgeon I've ever had!" This formidable being, white-haired and gruff, was called in consultation by my partner, when I had been with him only a month or two, and as always I was bidden to attend. In giving his opinion, he turned to me and said: "I think, Dr. Abercrombie, if you will do so and so . . ." DOCTOR Abercrombie! Had he really said "Doctor"? He had! By that single word, by that title, he acknowledged, indeed he welcomed, me as his colleague, and made it clear that at last we met on level terms. That is as it should be. When a consultant and a general practitioner meet, no matter how distinguished the one or how obscure or diffident the other, they meet on terms of absolute equality.—G. F. Abercrombie, V.R.D., M.D., The Art of Consultation, *The Practitioner*, January, 1959.

ARTIFICIAL HEMODIALYSIS IN MANAGEMENT OF GLUTETHIMIDE INTOXICATION

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Capt. Robert H. Herman, Capt. Melvin D. Cheitlin (MC), U. S. Army
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and
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Two patients attempted suicide by taking glutethimide (Doriden). Although the amount did not exceed 15 Gm. in either case, both patients went gradually into deep coma. Artificial hemodialysis was commenced in each case after conservative methods, including use of stimulants and diuretics, had failed. In one patient visible improvement began within three hours. In the other, deglutition and some reflexes were normal after eight hours of hemodialysis, but coma continued and tracheotomy was necessary to prevent asphyxia. In the latter patient, rather abrupt and complete recovery from coma occurred next day, 20 minutes after a diagnostic lumbar puncture. Quantitative data obtained from this patient showed that the diuresis had removed only small amounts of glutethimide, whereas the artificial hemodialysis had removed at least 1,420 mg. of the drug at an almost constant rate of 150 mg. per hour.

Although a recent arrival on the medical scene, glutethimide (Doriden), or 2-ethyl-2-phenylglutarimide, has become a widely used nonbarbiturate "non-habit-forming" sedative. Glutethimide has already joined a large list of drugs which have been used in suicidal attempts,[1] a considerable number of which have terminated fatally.[2]

Because of the structural similarity of glutethimide to phenobarbital (fig. 1) and the known renal clearance of the latter drug, it seemed logical to us that hemodialysis might prove to be lifesaving in those cases of glutethimide overdosage in which the patients are not responsive to conservative medical management. The purpose of this report, therefore, is to show how two such patients were successfully treated with artificial hemodialysis.

The patients were treated on the medical and neuropsychiatric services of Walter Reed Army Hospital. Glutethimide assay of serum, urine, and hemodialysate was performed by the method of Goldbaum and associates.[3] This method is based on the characteristic ultraviolet absorption spectrum of glutethimide and its rate of disappearance with hydrolysis in alcoholic potassium hydroxide. External dialysis was performed with the Kolff-Brigham rotating dialyzer.

Report of Cases

CASE 1.—A 19-year-old servicewoman was admitted to the neuropsychiatric service at Walter Reed Army Hospital on Aug. 10, 1955, because of paranoid schizophrenia. After several months of treatment, which included psychotherapy and chlorpromazine therapy, she improved sufficiently to be placed on an open ward and on occasion was allowed to leave the hospital.

On March 6, 1956, this patient went on pass from the hospital. She returned to her ward for supper and then went to bed. The following morning she could not be aroused. Deep tendon reflexes were active, corneal reflexes were present, vital signs were normal, and she responded to painful stimuli. After several hours her corneal reflexes disappeared, and she no longer responded to painful stimuli. Her belongings were searched, and an empty medicine bottle was discovered, as well as two physicians' cards. We learned by telephone that she had consulted these two doctors during the preceding afternoon for alleged insomnia. The second physician had given her a prescription for 30 tablets of glutethimide (500-mg. tablets) which she had had filled at a local drugstore. While these telephone calls were being made, blood and urine samples were checked but these showed no evidence of barbiturates. It was thought that the glutethimide could probably be excreted by promoting diuresis. The patient received 1,000 ml. of 5% glucose in water and 1,000 ml. of 5% glucose in saline solution over a six-hour period. She was also given a total of 55 mg. of methamphetamine, intramuscularly, in four divided doses. There was no response, and the deep coma continued.

At 1:30 a. m. on March 8, her pulse rate had increased to 128 per minute and her respirations were 44 per minute. She was given electric bulbar stimulation, which served only to increase her respiratory rate without change in her vital signs or state of consciousness. An endotracheal tube was utilized to provide the patient with a better airway. At 3 p. m. on March 8, 1956, she was transferred to the medical service.

She was still comatose on arrival on the medical ward and did not respond to painful stimuli. She had no corneal reflexes, but her deep tendon reflexes were active. Her pupils were dilated and equal and they reacted to light. Neurological examination was otherwise negative. Blood pressure was 94/40 mm. Hg; pulse, 116 per minute; respirations, 40 per minute; and temperature, 102 F (38.9 C) rectally. A urine specimen taken on admission to the medical service

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From the Department of Medicine, Walter Reed Army Hospital (Major Chandler, Captains Czarnecki, Herman, and Cheitlin), Department of Metabolism, Division of Medicine, Walter Reed Army Institute of Research (Lieutenant Colonels Meroney and Herndon), and Toxicology Department, Armed Forces Institute of Pathology (Dr. Goldbaum), Washington, D. C.

showed a trace of albumin and a specific gravity of 1.010 but was otherwise normal. Hemogram showed 19,600 leukocytes per cubic millimeter, with 85% neutrophils, and a hematocrit of 44. Blood urea nitrogen level was 8 mg. per 100 ml., carbon dioxide–combining power was 25.2 mEq. per liter; sodium level, 140 mEq. per liter; potassium level, 3.9 mEq. per liter; chloride level, 104 mEq. per liter. Another attempt was made at flushing out the glutethimide by means of a diuresis. Over a nine-hour period, 6,000 cc. of Ringer's solution and sodium lactate was given intravenously. During this time she excreted 3,500 cc. of urine. Picrotoxin, 11 cc., was given over a 40-minute period, but there was no change in her condition.

On March 9, at 3:30 a. m., her pulse rate was 128 per minute, respirations 44 per minute, blood pressure 100/55 mm. Hg, and her temperature 101.4 F (38.6 C) rectally. Her right lung field at the base was dull to percussion with almost absent breath sounds, which suggested that a pleural effusion had developed. Thoracentesis, however, resulted in only 30 cc. of straw-colored, slightly blood-tinged fluid.

Since there was no improvement in the patient's condition, a decision was made to perform an artificial hemodialysis. Consequently, at 4:15 p. m. on March 9 (approximately 70 hours after drug ingestion) dialysis on the Kolff-Brigham-type apparatus was begun. Three hours later the patient began moving about and shortly thereafter she vomited. At 9 p. m. she responded to painful stimuli and one and one-half hours later she opened her eyes and responded to simple oral commands. Hemodialysis was terminated at midnight.

Overnight her respirations decreased from 40 to 18 and her pulse rate to 72. Her temperature had dropped to 100.2 F (38.4 C). By 6 p. m. on March 10 she was able to resume oral administration of fluids. The following day she expressed further suicidal ideas and was transferred back to a closed ward of the neuropsychiatric service.

Case 2.—A 34-year-old married woman was first given a diagnosis in 1946 of postpartum paranoid schizophrenia. Her initial treatment was electroshock therapy which was followed by a remission until 1950 when her first exacerbation occurred. Hospitalization was not required, however, and she was treated on an ambulatory basis until November, 1956, at which time further hospitalization on the neuropsychiatric service was deemed advisable. She remained in the hospital until January, 1957, during which time she received up to 1.2 Gm. of chlorpromazine (Thorazine) per day with good results. She was apparently progressing satisfactorily until Feb. 11, 1957, when her husband returned home from work and was unable to arouse her. He found an empty bottle of glutethimide and estimated that the patient had ingested between 40 and 45 250-mg. tablets of this drug. She arrived in the emergency room and was admitted to the hospital at 7 p. m.

At the time of admission the patient was in a deep coma. She was limp and had slow shallow respirations at a rate of four per minute. Her blood pressure was 70/40 mm. Hg, and her pulse rate was 100 per minute and was regular but of poor quality. There was a peculiar reddish flush to the skin primarily involving the face, neck, and upper part of the chest. The pupils were widely dilated and nonresponsive to light. The corneal reflexes were absent. The deep tendon reflexes were hypoactive throughout. The ears, nose, and throat were normal. The chest was symmetrical. No rales were heard. The abdomen and extremities were normal. Admission urinalysis and hemogram were normal. Blood urea nitrogen level was 21 mg. per 100 ml., carbon dioxide–combining power, 25.2 mEq. per liter; sodium level, 143 mEq. per liter; potassium level, 4.3 mEq. per liter; and chloride level, 101 mEq. per liter.

On her admission to the medical ward an intravenous infusion of 5% glucose in water containing 10 mg. of phenylephrine was started. Because of her marked respiratory depression, including two episodes of apnea which required artificial respiration, the deep coma and hypotension, and our experience with case 1, we began preparations for artificial hemodialysis. Hemodialysis was started at midnight, Feb. 11, and ended at 10 a. m. on Feb. 12—a 10-hour dialysis. The clinical progress and the blood levels of glutethimide are shown in figure 2. During the dialysis, urine and dialysate samples were obtained for determination of their glutethimide content, and a slow progressive increase in the frequency and depth of respiration occurred. Hemoglobinuria was noted after two hours of dialysis, and serum hemoglobin level at that time was 130 mg. per 100 ml. Hemoglobinuria had completely cleared by 7:30 p. m. on Feb. 12, or 15 hours after it was first noted. Her blood pressure stabilized without vasoconstrictors after four hours. After eight hours her deglutition, corneal reflex, and pupillary reaction to light were normal. Toward the end of the dialysis, the patient responded to painful stimuli by withdrawing and groaning. At 2:30 p. m. on Feb. 12, four and one-half hours after completion of dialysis, the patient was still quite comatose; a Levin tube was passed and thick greenish material was aspirated from the stomach. This material contained 0.35 mg. per 100 ml. of glutethimide. Gastric aspiration had not been done previously during the hospital course. Tracheotomy was required at 11:30 p. m. because of retained pulmonary secretions. A diagnostic lumbar puncture was done at 11:30 a. m. on Feb. 13 because of the continuing coma. Twenty minutes after the spinal tap was done, the patient rather abruptly and completely recovered from the coma. She was transferred to a closed neuropsychiatric ward on Feb. 16 for further care.

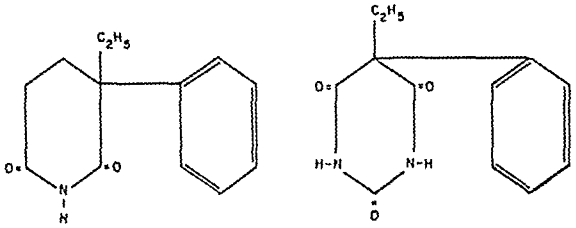

Fig. 1.—Comparative formulas showing structural similarity of glutethimide (Doriden) (*left*) and phenobarbital (*right*).

Comment

Our two cases of coma due to the use of glutethimide in suicidal attempts have demonstrated to us the value of artificial physical removal of the agent from the body when medical management fails to bring the desired response. Hemodialysis was considered worthy of trial because of the structural similarity of glutethimide to phenobarbital, and the well-known successful use of hemodialysis in cases of barbiturate poisoning,[4] as well as in bromide [5] and salicylate poisoning.[6]

Since glutethimide has been shown to be excreted, at least in part, in the urine,[7] it is probable that such a substance should be dialyzable by artificial means. The rate of removal of glutethimide is comparable to that of barbiturates; in case 2, it was removed at an almost constant rate of 150 mg. per hour when blood levels were 3.0 to 4.3 mg. per 100 ml. A total of 1,420 mg. of the drug was recovered from the dialysate fluid.

During the period of dialysis in case 2, urine flow varied from 7 to 32 ml. per hour. The concentration of glutethimide was fairly constant at 2.5 to 3.5 mg. per 100 ml. of urine, but at such a slow rate of flow, only 6.7 mg. was recovered from the urine formed during the 10 hours of dialysis. It is interesting to note that the patient had approximately the same urine concentrations of drug prior to dialysis; levels of 1.65 to 3.5 mg. per 100 ml. were found. Only 9.7 mg. of glutethimide was recovered from the urine formed during the five hours in the hospital preceding dialysis.

We believe that the lethal dose of glutethimide is lower than that originally reported. On the basis of the LD_{50} for mice, it has been estimated that the lethal adult human dose would be about 40 Gm.[8] However, McBay and Katsas have reported fatalities after the ingestion of as little as 10 Gm.[1d] Our series of two cases is admittedly small, but both patients demonstrated deep coma which was unresponsive to conservative management even though they had ingested only 10 to 15 Gm. of this drug.

The slowness with which the coma in our patients lessened is reminiscent of barbiturate intoxication. This probably is related to the slow rate of release of the drug from tissue sites and possibly from cerebrospinal fluid. Also, in case 2, there was an additional factor of importance—the presence of significant quantities of glutethimide in the gastrointestinal tract for as long as 26 hours after ingestion. Therefore the slow speed of fall in blood concentrations demonstrated by case 2 (fig. 2) was most likely a reflection of the slow release from tissue plus the continuing reabsorption from the gastrointestinal tract. This observation should again serve to stress the importance of thorough early gastric lavage in a patient who has ingested toxic quantities of glutethimide. Schreiner and co-workers have actually recovered portions of undissolved tablets of glutethimide 69 hours after their ingestion.[2a]

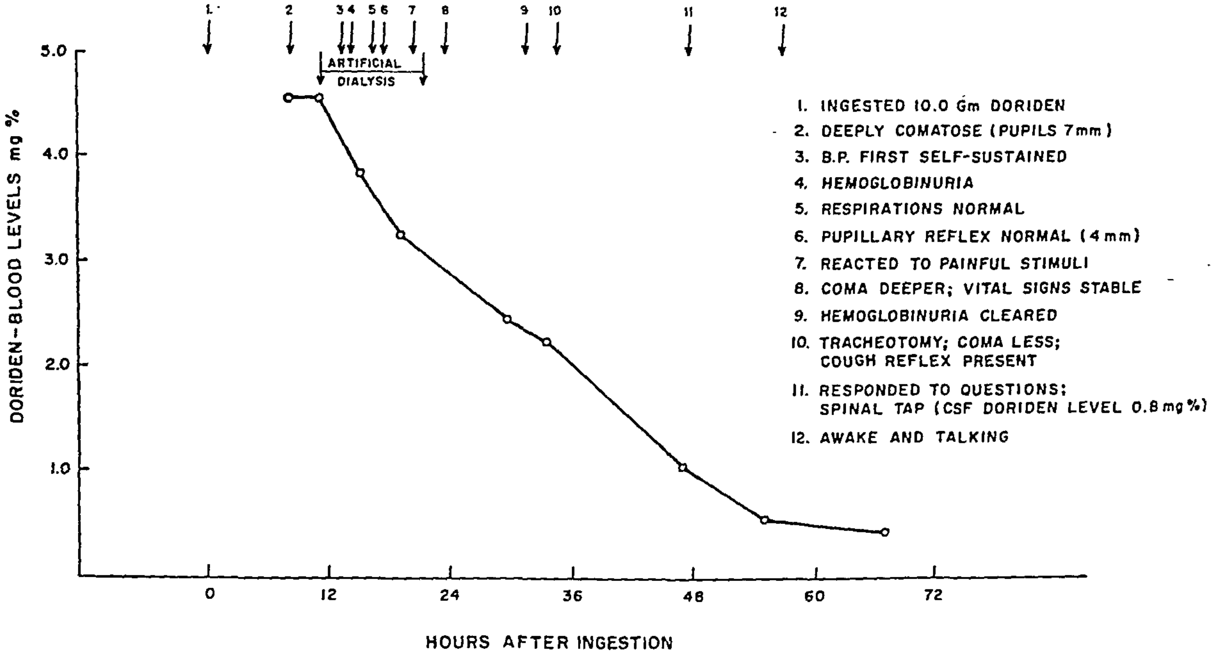

Fig. 2.—Changing clinical status correlated with glutethimide (Doriden) blood levels.

From the clinical standpoint, there were several physical findings of importance. Both patients were moderately hypotensive when first examined; the second patient required phenylephrine prior to hemodialysis to maintain her blood pressure. There was a peculiar blotchy bluish-red discoloration of the skin involving the blush area in the second patient. The respiratory exchange in both patients was markedly depressed, but in the first patient the respiratory rate was as high as 40 to 48 per minute (she had, however, received large quantities of methamphetamine), while in the second patient spontaneous breathing sometimes ceased, so that artificial respiration was required. This certainly would account for the retained secretions which eventually necessitated a tracheotomy in the second patient.

Cerebrospinal fluid was obtained shortly before the second patient regained consciousness and this showed a glutethimide level of 0.8 mg. per 100 ml., which demonstrated that there is no blood-brain barrier, at least at a plasma level of 1.0 mg. per 100 ml.

Conclusions

Artificial hemodialysis may be lifesaving in patients poisoned with glutethimide where medical management fails to bring the patient out of coma. In this respect, glutethimide joins barbiturates, salicylates, and bromides. The lethal dose would appear to be much less than that originally reported, for, without hemodialysis, we believe that neither of our patients would have survived after presumably ingesting 10 to 15 Gm. of glutethimide. Fatalities have been reported elsewhere on doses of as little as 10 Gm. of the drug. Prolonged or recurrent coma may be related to continuing absorption from the gastrointestinal tract. Therefore, gastric lavage should be done even though coma may have been present for 24 to 48 hours.

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PERITONEAL DIALYSIS

I. TECHNIQUE AND APPLICATIONS

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Complications of earlier methods of peritoneal dialysis are eliminated by a new technique of intermittent dialysis utilizing commercially prepared electrolyte solutions, special catheters, and a "closed system" of infusion and drainage. This was mechanically successful in 76 instances. Conditions treated satisfactorily included acute renal failure, barbiturate poisoning, intractable edema, hepatic coma, hypercalcemia, and chronic uremia. Although less efficient than the artificial kidney on an hourly basis, peritoneal lavage is easier to use over extended periods of time.

Although peritoneal dialysis was first used in human subjects with renal insufficiency in 1923,[1] it has never gained widespread popularity in the United States. This is attributable to the frequent complications (peritonitis, overhydration, electrolyte abnormalities, leakage, and drainage difficulty) reported by the early workers during prolonged, continuous peritoneal dialysis[2] and the development of effective artificial kidneys.[3] Treatment with an artificial kidney, however, remains a formidable and costly procedure. It is generally agreed that efficient and safe operation requires an active and permanent team of trained personnel and that this technique should be limited to relatively few hospitals serving large population areas.[4]

Our experience with a Kolff twin-coil artificial kidney at a university medical center would seem to reinforce these admonitions. The blood bank must always be prepared to furnish 5 units of fresh blood for priming of the kidney and for possible use during the procedure. Continuous heparinization of the patient, rapid changes in blood pressue, and variable movements of fluid between [illegible] and the bath solution require special [illegible] edge and techniques and the constant [illegible] of trained physicians and nurses. [illegible] do arterial and venous cut-downs [illegible]

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the catheters and should be immediately available in case of leakage or clotting, as well as at the end of the dialysis for surgical closure. Although the average length of dialysis is six hours, gathering of the necessary personnel, preparation of the machine and patient, and cleaning up afterward generally require another three to four hours. It would be difficult to visualize operating an artificial kidney in the usual, smaller private hospital with less elaborate facilities, where its use would be indicated infrequently. Yet most of the hospitals in the United States are in this category.

For these reasons, over the past three years we have explored the potentialities of peritoneal dialysis.[5] Modifications of Grollman's intermittent procedure [6] have eliminated almost all of the previously reported difficulties and complications. We believe that the modified procedure can be used efficiently and safely without specialized knowledge of fluid and electrolyte metabolism or intricate laboratory facilities. Direct comparison of results in patients with renal failure have proved it to compare favorably with dialysis with the artificial kidney.[7] The present report describes our technique of intermittent peritoneal dialysis and its application in a variety of clinical circumstances.

Technique

Solutions.—Although previous authors have advocated extemporaneous preparation of the lavage fluid from commercially available solutions,[8] we have found this to be arduous and unsatisfactory. Most hospital pharmacies do not stock the necessary anhydrous magnesium and calcium chloride. The pH must be accurately adjusted and the sodium bicarbonate added separately, or precipitation of calcium salts may occur. Caramelization and discoloration of the dextrose-containing solution may take place during autoclaving, and adequate sterilization is seldom assured. Solutions are now prepared commercially and may be stocked in ordinary liter infusion flasks in the hospital pharmacy, together with special Y-type administration tubing and sterile catheters. A dialysis thus can be started within 30 minutes after the decision is made.

TABLE 1.—*Composition of Dialysis Solution*

	mEq./Liter	Gm./Liter	mOsm./Liter
Sodium	140.0		140.0
Chloride	101.0		101.0
Calcium	4.0		2.0
Magnesium	1.5		1.0
Lactate	45.0		45.0
Dextrose		15.0	83.0
Total	291.5*		372.0†

* Addition of 4 mEq. per liter of potassium chloride, when indicated, increases this to a normal value of 300 mEq. per liter.

† Theoretical osmolality Measured total osmolality by freezing point determination is 349 mOsm. per liter, compared with measured values in normal human subjects of 280 mOsm. per liter.

The composition of the dialysis solution is shown in table 1. It is essentially an idealized potassium-free extracellular solution with enough dextrose added (1.5%) to increase the osmolality to 372 milliosmols (mOsm.) per liter, somewhat higher than the levels we have found in uremic patients. This prevents absorption of administered fluid from the abdomen and the overhydration frequently reported after earlier procedures.[9] Potassium is omitted because dialysis is often performed to correct hyperkalemia. When it is used for barbiturate poisoning or in other situations in which there is a normal serum potassium level, potassium chloride can be added as a concentrate by hypodermic syringe to bring the concentration to 4 mEq. per liter.

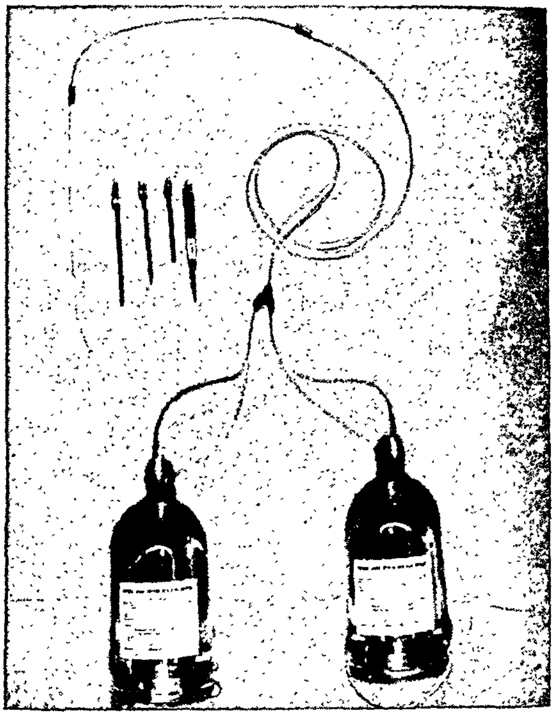

Fig. 1.—Equipment for peritoneal dialysis. Two liters of electrolyte solution are shown, with administration tubing attached to special catheter. Also shown is Duke trocar set, consisting of straight trocar with sharp and blunt stylets and scalpel with no. 11 Bard-Parker blade.

Since crystalloids diffuse in both directions across the peritoneal membrane,[10] any biochemical abnormalities in the patient's serum will be partially corrected by the use of a solution containing "normal" concentrations of all the physiologically important electrolytes. To alter the solutions according to the individual patient's specific electrolyte pattern is hazardous in most hands and contributes little to the over-all clinical results. In 76 peritoneal dialyses, we have never caused hyperchloremia or any other of the acid-base imbalances which have complicated previous procedures. The magnesium concentration of 1.5 mEq. per liter is within the lower normal range for humans. Although 4 mEq. of calcium per liter is higher than the ionized fraction in the blood, many of the patients have hypocalcemia, and whatever calcium is absorbed will be partially bound in the serum by protein; this level of calcium in the dialysis solution has never caused digitalis intoxication in any of our digitalized patients.

Since 2 liters of solution are given simultaneously, with immediate mixing within the peritoneal cavity, additional drugs or electrolytes need only be inserted into one of the bottles, lessening the chance of bacterial contamination. To each 2 liters of solution are added 25 mg. of tetracycline, 8 mEq. of potassium chloride (if the serum potassium level is not elevated), and 10 mg. of aqueous heparin. The use of heparin is discontinued after three exchanges if the outflow fluid is not grossly sanguineous.

When a peritoneal dialysis is performed for the relief of intractable edema, a hypertonic solution with identical concentrations of electrolytes but with 7% dextrose (versus 1.5%) is used, having an osmolality of 661 mOsm. per liter. This results in marked negative fluid balance during the procedure. Ten per cent dextrose (842 mOsm. per liter) has also been used for this purpose.

Materials.—The necessary equipment (fig. 1) consists of an ordinary paracentesis set with a straight 17 F. Duke trocar set, suitable quantities of dialysis solution with tubing, and sterile catheters. After experimenting with plastic catheters of various types, it was found that the most suitable is a fairly rigid nylon catheter, 11 in. long, slightly curved at the distal end, with a solid, rounded tip (fig. 2). The distal 3 in. is perforated with multiple smooth holes of very small diameter (80 perforations, 0.02 in. in diameter). The external diameter of the catheter is 0.136 in. and is made to fit snugly into a 17 F. metal trocar.

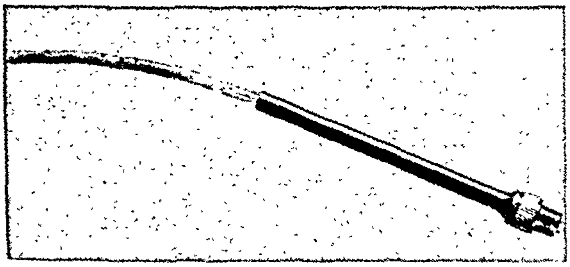

Fig. 2.—Nylon catheter and trocar. Note multiple small perforations, permanent curve, and rounded tip at distal end of catheter.

Perhaps the single greatest complication in the past has been difficulty in obtaining adequate outflow. This led various workers to utilize inflow and outflow tubes through two separate abdominal incisions, to devise elaborate sump pumps for negative-pressure drainage, and to insert the tubes under direct vision in the operating room.[11] In retrospect, inadequate drainage resulted from (*a*) clinging of the omentum and intestines around the irritating metal and rubber tubes, (*b*) fibrin clots within the outflow tube, and (*c*) most important, plugging of the tube with tiny bits of omental fat sucked into the lumen through the perforations. The use of nonirritating plastic catheters and the addition of adequate heparin to the inflow solution has eliminated the first two factors. The simple expedient of greatly reducing the diameter but increasing the number of the multiple distal perforations has successfully prevented particles of omentum from entering the catheter and permitted the use of simple, smooth catheters rather than more costly double-lumened or grooved tubes.[12]

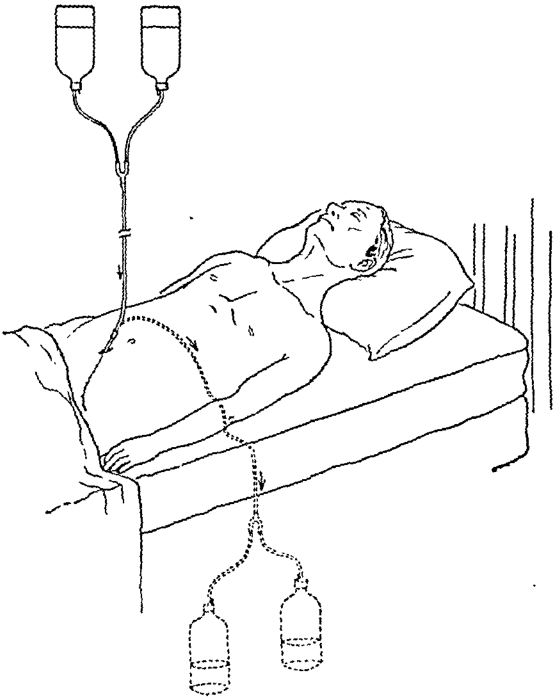

Fig. 3.—Peritoneal dialysis procedure. (See text for details.)

Procedure.—The patient should be supine or semisupine with his bladder emptied just prior to the procedure. No special sedation is necessary unless the patient is unduly apprehensive or agitated. The abdomen is shaved, prepared, and draped as for a laparotomy. After local infiltration with procaine hydrochloride, an incision is made in the midline about one-third of the way from the umbilicus to the pubic bone. The incision should be small enough so that the skin fits very snugly around the trocar. The scalpel blade (no. 11 Bard-Parker) is inserted into the anterior abdominal wall until it is felt to "grate" on the linea alba, and a small incision is made in the latter. The midline is relatively avascular, and any slight superficial bleeding which occurs is usually controlled by lateral pressure exerted by the trocar and catheter.

The trocar, with the stylet in place, is inserted through the incision into the peritoneal cavity. At times, a sharp thrust is necessary, and the patient may experience some pain as the peritoneum is stretched. When the peritoneum has been pierced, with the stylet removed the trocar should easily slide in to its full length, so that only the proximal hub protrudes above the skin. In very thin individuals, we have occasionally distended the abdominal cavity with 2 liters of dialysis solution infused through a large-bore (no. 15) hypodermic needle before attempting insertion of the trocar.

The plastic catheter is then fitted through the trocar. The permanent curve at the end of the catheter and its relative rigidity permit it to be manipulated by rotation from the proximal end, much as is done during cardiac catheterization. It also prevents kinking or floating of the catheter to the surface within the abdomen. The rounded tip minimizes injury to the abdominal contents. The direction of the catheter can also be altered by angling the entire trocar in any direction. The catheter is aimed dorsally and toward the left or right lumbar paravertebral sulcus. It is at times necessary to rotate it in various directions, trying to insert it each time, before omentum is pushed aside or a natural pathway is found. Ideally, the catheter should extend well into the peritoneal cavity. On a few occasions, when complete insertion seemed impeded (by adherent omentum), 1 or 2 liters of solution was allowed to run in and the catheter was subsequently readjusted.

The trocar is then withdrawn and the catheter connected to the Y-tubing, which has been previously connected to 2 liters of dialysis solution warmed to body temperature. Necessary drugs (tetracycline, heparin, etc.) are added in advance. The solution is permitted to flow into the abdominal cavity by gravity as rapidly as possible, ordinarily taking between 5 and 10 minutes for completion. If the fluid flows in more slowly than this, the catheter should be repositioned, as its tip may be buried in omentum.

When the bottles are empty but the tubing is still filled with fluid, the tubing is clamped and the bottles are placed on the floor beside the patient's bed. The fluid is permitted to remain within the abdominal cavity for one hour, after which the clamp is removed and the abdomen is drained by a siphon effect through the closed system back into the original two bottles. If the system is patent, gravity drainage should occur rapidly and steady forceful streams of fluid should be seen entering each of the bottles. When the flow slows down and becomes a steady drip, manual compression of the abdomen toward the catheter may cause resumption of steady flow for a short while. Drainage should take no more than 10 minutes. Since the liter flasks are graduated in both directions, precise fluid balance can be ascertained at a glance.

Just before drainage is begun, 2 liters more of solution with fresh tubing are prepared, so that as soon as drainage ceases a new infusion can be started. This is repeated continuously for from 12 to 36 hours, depending on the purpose of the dialysis and the number of exchanges desired. Usually between 30 and 50 liters is exchanged. A careful protocol is kept, listing exact time for starting and ending each exchange, drugs added, vital signs, and fluid balance. Ideally, after the first few exchanges intermittent peritoneal dialysis can become a nursing procedure, with the physician called only if there is difficulty with fluid balance or any untoward complication.

The most frequent complication of peritoneal dialysis reported in the literature has been peritonitis.[13] In our experience, clinical peritonitis has never occurred, and 43 cultures of peritoneal fluid sampled at the end of dialyses have all been sterile. Furthermore, in 16 autopsies performed on patients who had undergone one or more peritoneal dialyses in the month prior to death, there was no evidence of peritoneal irritation or bleeding, except for local hematomas of the mesentery in one patient who had a uremic bleeding tendency. The threat of peritonitis has been eliminated by (*a*) the use of an essentially closed technique with the dialysis fluid drained into the original bottles, (*b*) the use of new sterile tubing with each infusion, (*c*) the addition of a broad-spectrum antibiotic to the solution, and (*d*) limitation of the procedure to a maximum of 36 hours.

Complications.—Sometimes abdominal pain is encountered, particularly toward the end of the outflow period. It is invariably ameliorated by instillation of the next inflow fluid, but, if the pain is severe, it can be treated with 5 cc. of 2% procaine hydrochloride instilled through the catheter into the peritoneal cavity. Restlessness and/or pain may require injections of meperidine (Demerol) or a short-acting barbiturate. Blood-tinged fluid is not uncommon during the first few exchanges and is caused by subcutaneous bleeding incident to the incision; if it persists, a purse-string suture pulling the adjacent skin and tissues around the catheter shaft may help. Severe bleeding has never occurred in our series.

Omentum or intestine which is adherent to the anterior abdominal wall or adhesions from previous abdominal surgery may prevent catheter insertion or result in poor drainage from loculated cavities. We were unable to perform dialyses in six patients, five of whom had widespread adhesions. In one patient who was extremely obese and in two patients with previous abdominal surgery and adhesions, the catheter was successfully inserted in the McBurney area on the right or in the corresponding point on the left side without difficulty.

At times, leakage around the catheter occurs. As with subcutaneous bleeding, a purse-string suture halts this complication. The original incision is intentionally made as small as possible to prevent leakage. It is preferable not to suture the catheter to the skin, so as to be able to manipulate it if necessary.

If the outflow stream slows down or stops, slight twisting or remanipulation of the catheter tip sometimes restores adequate flow. If this maneuver fails, 20 cc. of saline solution can be forced through the catheter under pressure from a syringe in an attempt to clear fibrin clot. Should this be unsuccessful, the catheter should be withdrawn and inspected; if obstructed by clot, it can be replaced with a fresh catheter along the original path. For this purpose, it is well to have a second sterile trocar available. If drainage is rapid but incomplete because of absorption of fluid, the solution may be made more hypertonic by the addition of from 50 to 200 cc. of 50% dextrose to each 2 liters until the desired negative balance is achieved. If this is necessary for more than a few exchanges, it is preferable to use 1 liter of 1.5% dextrose and 1 liter of 7% dextrose solution for each exchange, since the addition of dextrose in water to the stock solution dilutes the electrolytes accordingly.

Abdominal distention and/or ileus has not been prominent, and, in the few cases in which it occurred, has disappeared within 24 hours after the procedure. Local edema of the anterior abdominal wall may be encountered if the catheter is not inserted far enough so that all of the perforations are within the peritoneal cavity. In a very thin person, or when the proximal end of the catheter extends more than 2 or 3 in. above the skin surface, part of the protruding end may be cut off with a sterile scissors.

When very hypertonic (7 to 10% dextrose) dialysis solution is being used to achieve negative fluid balance, there may be a sudden decrease in blood pressure. This is caused by temporary hypovolemia from the rapid movement of fluid from the vascular compartment into the peritoneal cavity; there is a lag in the replacement of this plasma volume from the interstitial tissues. If this occurs, loss of fluid can be slowed down by using a solution with less dextrose (and less osmotic pressure). The immediate treatment is restoration of vascular volume by the infusion of salt-poor human albumin or whole blood. When using hyperosmotic solutions, we have adopted the practice of diluting 25 Gm. of albumin in 500 cc. of 5% dextrose in water and infusing this at a slow rate throughout the dialysis. Hypotension can then be corrected as necessary by increasing the rate of infusion.

Contraindications.—Infection of the peritoneal cavity is an absolute contraindication to peritoneal dialysis. Recent or extensive abdominal surgery is a relative contraindication, although we have successfully dialyzed three patients after cholecystectomy, abdominal aortic resection, and appendectomy, five, eight, and six days after surgery respectively.

Report of Cases

CASE 1 (Acute Renal Failure).—A 35-year-old man with severe oliguria and heart failure associated with Staphylococcus aureus bacterial endocarditis was seen in consultation in another hospital. An electrocardiogram showed evidence of grave potassium intoxication (loss of P waves, QRS interval 0.24 second, bradycardia), and the patient had pulmonary edema with cardiac asthma. An infusion of 50% dextrose in water with added insulin and calcium gluconate was started via a femoral vein catheter into the inferior vena cava until the patient could be transferred to the medical center of the University of California at Los Angeles, where he underwent peritoneal dialysis for 27 hours with a mildly hypertonic, potassium-free solution. Predialysis and postdialysis values are shown in table 2.

TABLE 2.—*Data Before and After Dialysis in Patient with Acute Renal Failure*

	Before	After
Potassium	9.2 mEq./L.	5.6 mEq./L.
Sodium	118.0 mEq./L.	129.0 mEq./L.
Chloride	77.0 mEq./L.	85.0 mEq./L.
Creatinine	17.8 mg./100 cc.	9.1 mg./100 cc.
Body weight	63 kg. (140 lb.)	60 kg. (134 lb.)

Within four hours after dialysis was started, P waves appeared on the electrocardiogram, the QRS interval decreased to 0.12 second, and the heart rate accelerated from 54 to 86 beats per minute. The lungs became less congested and the patient improved markedly. Despite a daily urine volume of less than 300 cc. for eight days after dialysis, the serum potassium level never increased to more than 6.7 mEq per liter, and the patient recovered uneventfully with conservative therapy. On hospital discharge, his blood culture was negative and his blood urea nitrogen level was 21 mg. per 100 cc.

Comment.—Peritoneal dialysis successfully reversed potentially fatal hyperkalemia and served the ancillary purposes of reducing pulmonary edema and improving uremia. The patient's weight before and after dialysis correlated closely with a measured negative fluid balance of 3.2 liters during the procedure. The use of an artificial kidney would have required prolonged intravascular catheterization in a patient with active bacterial endocarditis.

CASE 2 (Intractable Anasarca).—A 28-year-old man was admitted to the hospital for refractory congestive heart failure and possible cardiac surgery. He had progressive heart failure which started at the age of 15 after an attack of rheumatic fever three years previously but had improved after a mitral valvulotomy at age 23. After a recurrence of active rheumatic fever two years prior to this hospital admission, his course had been downhill, with intractable left-sided and right-sided heart failure, despite rigid sodium restriction and use of digitalis and diuretic agents. Heart sounds and cardiac catheterization studies indicated recurrence of mitral stenosis and possible tricuspid stenosis, but cardiac surgery could not be performed because of the patient's poor clinical status and increasingly frequent attacks of pulmonary edema.

Peritoneal dialysis was started with the hypertonic (10% dextrose) solution and was terminated after eight hours because of a sudden episode of continuous coughing followed by acute pulmonary edema. This may have been precipitated by diaphragmatic irritation from the hypertonic dialysis solution, since the patient complained of pain in the left shoulder which was worse on inspiration. Fluid balance during the eight-hour dialysis was as follows: total fluid in, 12,000 cc.; total fluid out, 20,500 cc.; negative balance, 8,500 cc. Two of the 8.5 liters removed consisted of ascites at the start of the procedure. The patient's weight fell from 74 to 65 kg. (163 to 143 lb.), with marked subsequent clinical improvement and further weight loss. He underwent successful mitral valvulotomy several weeks later and is at the present time completely symptom-free without edema and pursuing an active life.

Table 3.—*Serial Electrolyte Values in Patient with Hypercalcemia*

Date, 1958	Therapy	Calcium, Mg./ 100 Cc.	Carbon Dioxide, mEq./ Liter	Sodium, mEq./ Liter	Chloride mEq./ Liter	Blood Urea Nitrogen, Mg./ 100 Cc.
1/31........	None	25.6	45.0	137.4	80.8	70.1
2/ 1........	Hydration	22.2	28.0	107.0	71.1	63.0
2/ 2........	Dialysis	10.4	28.2	126.0	86.0	33.0
2/ 7........	Follow-up	9.4	26.2	136.0	110.0	16.0

Comment.—Despite ending the peritoneal dialysis prematurely, considerable edema fluid was removed. A subsequent further spontaneous diuresis after mechanical mobilization of edema in intractable heart failure has been reported previously.[14] Some degree of diaphragmatic irritation as manifested by shoulder pain has occurred in several patients during the use of 10% dextrose solution. It does not usually preclude continuation of dialysis. This patient's heart was so incompetent, however, that the physical exertion of repeated coughing initiated acute pulmonary edema. It was the opinion of all concerned that cardiac surgery would have been impossible without the dialysis.

Case 3 (Hepatic Coma).—A 23-year-old woman developed homologous serum hepatitis two months after a series of injections of penicillin. Despite adequate therapy and bed rest, her jaundice steadily increased, she developed fetor hepaticus, the area of liver dulness disappeared, and she became deeply comatose. The serum bilirubin level was 46 mg. per 100 cc., and the prothrombin time was less than 10% of normal. Peritoneal dialysis was employed as a desperate measure after six days of unremitting coma. During 38 hours, 56 liters of fluid was exchanged. Four hours after the termination of the procedure, the patient became perfectly lucid, despite an essentially unchanged serum bilirubin level. She maintained her clinical improvement for five days, after which she became progressively worse; one week later she died in hepatic coma with hypotension and moderate terminal uremia. A second dialysis attempted on the day before death did not alter her clinical state. Autopsy revealed hepatic necrosis (liver weight 860 Gm.) with hemorrhagic regions in all organs, including the heart.

Comment.—It appeared more than coincidental that the patient abruptly recovered from eight days of deep coma after dialysis. As expected, the large bilirubin complex equilibrated poorly with the peritoneal contents, but the failure of "direct" bilirubin to cross the peritoneal membrane was unexplained. Unfortunately, arterial ammonia determinations were not performed before or after dialysis. The response of this patient and others[15] would seem, however, to indicate that hepatic coma may be partially caused by an unknown dialyzable substance.

Case 4 (Hypercalcemia).—A 49-year-old woman with sarcoidosis had been treated for six months with prednisone, 40 mg. daily, for tracheal constriction and for three months with large quantities of calcium carbonate (15 Gm. per day) because of a previous peptic ulcer. She developed weakness, vomiting, muscle pains, and restlessness and was admitted to the hospital. On the day of admission her serum calcium level was reported as 20 mg. per 100 cc. Prednisone therapy was continued, use of calcium carbonate was stopped, and intravenous hydration was attempted. Despite these measures, she became comatose, with loss of deep tendon reflexes.

Twenty-four liters of calcium-free dialysis solution was exchanged over a period of 15 hours. Serial electrolyte values are shown in table 3. It can be seen from the data that hydration, while decreasing the calcium level slightly, dangerously diluted all the serum electrolytes. Dialysis, while removing a measured 1,864 mg. of diffusible calcium, also partially corrected the hyponatremia, hypochloremia, and uremia. The patient improved clinically following dialysis; when last seen (on July 9, 1958) she had normal electrolyte values.

Comment.—This patient became comatose from severe hypercalcemia incident to sarcoidosis and excessive absorption of ingested calcium carbonate. She was moribund and appeared to be in preterminal condition. A possible therapy for this situation would have been the administration of adrenal steroids, but the patient had been taking prednisone for several months (she had clinical evidence of the treatment of the edema of thrombophlebitis and migratory phlebitis. Fifty-one cases of thrombophlebitis treated with buccally administered proteases have been reported.[12] Reponse to treatment was excellent or good in all but one case. In acute thrombophlebitis treated with buccally given streptokinase for three to four days, the usual pattern is a loss of pain, tenderness, and overlying redness and edema in about 48 hours after initiation of treatment. Ambulation is generally possible and permitted in about 72 hours without deleterious effect. Chronic thrombophlebitis cases may require slightly longer treatment, averaging eight days. There is no contraindication to the concomitant use of anticoagulants.

An illustrative case is that of a woman, aged 84, with acute iliofemoral thrombophlebitis. Absolute bed rest and tetracycline therapy caused no appreciable change in four days. Buccal therapy with streptokinase was started and continued for 10 days. Within six hours the patient could move the leg more freely and there was considerably less discomfort and pain along the involved venous segment. Edema and erythema were significantly less in 24 hours. The patient was ambulant by the fourth day of treatment.[12]

A diagnosis of chronic thrombophlebitis was made in a patient with a complaint of tenderness and pain in the lower left leg for six months. The only treatment administered was streptokinase buccally for four days, after which there was marked decrease of edema and complete relief of pain.[8] Three cases of migratory phlebitis have been successfully treated with buccally given streptokinase, two with excellent results and one with good results.[12]

The success of buccal protease treatment for thrombophlebitis correlates with the degree of inflammation present. Removal of the inciting factor, the thrombus, necessitates much higher enzyme dosage, usually 10 to 100 times that found effective for anti-inflammatory activity, and is best administered intravenously.

Edema Incident to Surgical Procedures.—Due to their activity in eliminating inflammatory sequelae, buccally given proteases have proved a useful adjunct to surgery, both therapeutically and prophylactically. Reduced edema, induration, and inflammation permit better approximation of tissue, less scar formation, faster healing, and less pain and discomfort for the patient. Buccally given streptokinase has been used as an adjunct in dental surgery,[13] mouth and face surgery, emergency craniectomy, amputation of gangrenous toes, diabetes mellitus, and surgical treatment of pilonidal cysts.

A study of 62 patients, 49 treated with buccally given streptokinase and 13 controls, ranging in age from 12 to 67 years, has revealed the effectiveness of this treatment in inflammation resulting from removal of impactions, apicoectomy, apicocurettage, multiple extractions, and predental surgery.[13] These procedures might be expected normally, even in the light of good surgical procedure, to produce pain, edema, trismus, or inflammation. Patients were followed postoperatively for intervals of 24, 48, and 72 hours. The patients to be treated were given tablets in the dosage of 20,000 units of streptokinase to be taken every four hours. At 24 hours, 5 of the 49 patients treated with streptokinase showed moderate edema, while 11 of the 13 controls showed moderate to severe edema. At 48 to 72 hours postoperatively, only 9 of the 49 patients treated with streptokinase showed more than slight edema and 1 patient complained of severe pain accompanied by minimal edema. Ten of the 13 controls showed considerably prolonged edema at the same period, while 2 who had only slight pain and edema without trismus at 4 hours showed good healing by 48 hours. Two controls who had severe inflammatory effects were given streptokinase and showed exceptional recovery within 24 hours. It is of interest to note that the streptokinase-treated group included a woman who was in the seventh month of pregnancy, a hemophiliac, two diabetics, two patients with a history of rheumatic fever, one with hypertension, one with syphilis, one with chronic arthritis, and four patients with allergies. No side-effects or toxicity were noted in these cases.

After the removal of a carcinoma from the floor of the mouth, the patient received streptokinase buccally with excellent results. Edema did not form at the site of operation and healing occurred rapidly.[5] In another patient streptokinase was administered buccally for three days after the resection of the lower lip with advancement of the vermilion border. Immediately postoperatively a minimal amount of edema was present, which disappeared in 24 hours. Healing occurred rapidly.[5]

Prophylactic use of buccally given proteases to prevent edema and inflammatory developments is a promising new application. It has been effective when used prior to eye enucleation, to dental surgical procedures, and to craniectomy for brain surgery. Clinical investigations are under way on the prophylactic use of buccally given streptokinase in catheterization of veins with indwelling polyethylene tubes. Kolman reported interesting new applications for this drug in urology. Postcystoscopic urethral edema and stricture formation were *significantly decreased in patients treated with* streptokinase.

Liquefaction and Localization of Acute Infections

In animal studies, Sherry and associates [14] have shown that the local injection of streptodornase into sites of pleural exudation produces a rapid degradation of desoxyribonucleo-protein and is often associated with a striking clinical improvement of the local area of infection. Ungar and Ginsberg [15] described the effect of parenteral administration of trypsin on the tissue response to implanted surgical gut in the liver. In the rabbits treated with parenterally given trypsin, the ring of granulation surrounding the surgical gut was significantly narrower than that of the controls. I reported the effects of parenterally given proteases on croton oil and staphylococcic-induced abscesses in rabbits. Rabbits treated with saline solution developed thick, purulent exudates after 48 to 72 hours. Rabbits treated with streptokinase showed marked clearing of interstitial edema and thinned inflammatory infiltrates.

Abscesses.—Reports have appeared concerning 30 patients with abscesses treated with buccally given streptokinase and antibiotics. Excellent results were obtained in 27 patients, good results in 2, and no effect in 1. In a series of patients with cellulitis excellent response was obtained in 33 patients and good response in 6. Of the latter, four had combined carbuncles and cellulitis. It is important to point out that in these reports antibiotics were used along with the enzyme.

A recent study [16] comprised 87 patients attending an outpatient clinic of a large municipal hospital. Each had evidence of an active, localized infection involving the skin, scalp, or lip. In a vast majority of instances the offending organism was Staphylococcus aureus. Other organisms encountered were beta-hemolytic streptococci, Staph. albus, Escherichia coli, Bacillus subtilis, Aerobacter aerogenes, and Pseudomonas. In two instances no bacterial growth was obtained. Treatment was limited to buccally given tablets containing 10,000 units of streptokinase every four hours.

Within 48 hours the abscesses had shown evidence of adequate resolution or sufficient liquefaction and localization to permit incision and drainage, which was done in most instances. Irrespective of the duration of the infection, once buccal streptokinase therapy was instituted, one could predict that within 24 to 48 hours there would be complete resolution or sufficient softening and localization to warrant a simple incision and drainage. *Buccal enzyme therapy was then continued* for an additional 24 to 72 hours to ensure uneventful healing. The quite remarkable localization effect of protease therapy upon acutely infected tissue casts considerable doubt upon the unsubstantiated view that buccal protease therapy affects the densely fibrinous "pyogenic" membrane. If this were so, local spread of infection and, indeed, bacteremia would follow protease therapy. Since the physiological effects comprised rapid localization and liquefaction, it is probable that proteases diffuse through, rather than hydrolize, the pyogenic membrane; the hydrolytic effect is upon the contained exudate, with resultant liquefaction.

Respiratory Tract Infection.—The buccal use of streptokinase provides a convenient method for managing some types of pulmonary inflammation such as chronic bronchitis, bronchiectasis, empyema, and pleural fistulas. Nine cases of chronic bronchitis were treated with buccally given streptokinase.[12] Two responses were excellent; seven were good. Thinning of thick secretions of bronchiectasis was observed in four out of seven cases treated. One patient with a pleural fistula that had been draining for many months responded with closure after treatment with buccally given streptokinase.

In another study protease therapy was used in patients with thick tenacious respiratory secretions.[17] The following effects were observed: 1. The sputum became thinner, more abundant, easier to raise. 2. The cough became more loose, more productive. 3. Accelerated granulation occurred in bronchial ulcerations and bronchial pleural fistula tracts. 4. In chronically ill patients, there appeared weight gain, improved appetite, improved sleep, and sense of well-being. 5. Acutely ill patients showed rapid resolution of inflammation with early subsidence of cough and substernal burning.

Acne Vulgaris.—An interesting and provocative use of streptokinase in acne vulgaris has been reported.[12] In six such patients, five showed excellent results and one responded well. The convenience of the buccal route lends itself to the management of this common complaint.

Decubitus Ulcers.—Batterman has reported excellent responses to buccally given streptokinase in previously refractory cases of decubitus ulcer.

Side-effects of Buccal Protease Therapy

No significant local or systemic reactions have been observed to follow buccally given streptokinase tablets. In about 10 to 15% of patients on therapy with buccally given trypsin tablets, there is evidence of mucosal irritation. In 270 patients treated, 7 instances of slight to mild glossitis have been reported. Systemically the sole side-effect after buccal protease administration was an occasional mild gastrointestinal disturbance characterized by moderate fulness or rumbling of brief duration.[12] The pyrexia and anaphylactic reactions encountered on intramuscular administration of proteases have not been observed with buccal enzyme treatment. Although no adverse reports have been made, caution should be exercised in the use of protease therapy in patients with blood-clotting deficiencies.

Mode and Site of Action

The primary mechanism underlying the experimental and clinical effects of proteases involves the diffusion or adsorption of plasminogen activators to the fibrin in thrombi or acutely inflamed tissue, with activation of intrinsic thrombus or fibrin plasminogen into plasmin. Small doses of buccally given proteases appear to combine with salivary plasminogen to form plasminogen activator which diffuses through the buccal mucosa in quantities sufficient to activate fibrin plasminogen into plasmin. It is of paramount importance to recognize that modification of acute inflammation, after buccal protease therapy, is related to the local formation of plasmin at the site of acute tissue injury. The cardinal indication for buccal protease therapy, therefore, is localized inflammation. This includes boils, abscesses, thrombophlebitis, respiratory tract infection, traumatic edema, hematomas, acne vulgaris, and many other conditions. Antibiotics remain the treatment of choice in nonlocalized inflammation.

Clinical utilization of buccal protease therapy provides a tool for modifying deleterious effects of developmental and reparative phases of the inflammatory reaction in locally injured tissue. Excessive exudate accumulation can be curtailed; edema fluid can be thinned and drained; tissue permeability can be restored; rapid localization and liquefaction of infected areas can be achieved. In a word, injurious host response to phlogogenic stimuli may be significantly modified by buccal protease therapy.

Summary

There are experimental and clinical disorders in which host defensive or reparative responses result in excessive tissue edema, destruction, or suppuration. In such disorders the intensity of host response constitutes the disease process. Rapid modification and control of the extent of inflammation follows buccal protease therapy due to three physiological effects: modified host response in hypersensitivity states, decreased tissue edema, and localization and liquefaction of exudates.

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IMPORTANCE OF HIDDEN "PLUS VALUES" IN EMERGENCY RESECTION FOR GASTRIC HEMORRHAGE

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The patient with severe hemorrhage from the upper gastrointestinal tract presents an urgent and difficult problem, especially as to the choice between conservative medical and direct surgical measures. The authors believe that there is justification for prompt laparotomy when the bleeding is massive, and they recommend that subtotal distal gastric resection be carried out even if exploration fails to locate the source. This operation was done in 21 patients, and in 5 no abnormality of esophagus, stomach, small intestine, or liver could be found. As a group, these 21 patients had the advantage of prompt definitive surgery instead of delay and can face the future with relative certainty that they will be free from subsequent ulcer formation and hemorrhage. A careful diagnostic program is assumed to precede such intervention. There were two deaths in this series. The mortality compares favorably with that reported for similar cases managed conservatively.

Although a few earlier surgeons, most notably Finsterer,[1] have for many years advocated and practiced emergency gastric resection for the control of massive gastroduodenal bleeding and the saving of life, it is actually within the past decade that this approach has been repeatedly proved to be a sound one. Simultaneous articles by Warren and Lanman [2] and by Hoerr, Dunphy, and Gray [3] in 1948 helped to bring the problem clearly into focus by enunciating most of the principles upon which the rationale of such emergency treatment rests today. Warren and Lanman took note of the inadequacy of nonsurgical methods of treatment by pointing out that, of each 20 patients admitted to the hospital with massive hemorrhage from peptic ulcer, 1 or 2 will die under conservative management and that in patients past middle life the mortality rises to a level between 20 and 33%. Hoerr and associates were among the first to advocate the free and early use of x-ray for localization of the bleeding lesion and suggested criteria to be used in the selection of patients for such emergency operations.

It remained, however, for Crohn,[4] writing with great candor and with the authority of a distinguished medical expert, to lend to the emergency surgical approach the type of support needed to establish it as a practical measure superior to other methods. He pointed to an unsatisfactory gross mortality rate of 10.3% in 2,800 medically managed patients and stated: "It is becoming increasingly clear that a completely passive attitude toward upper gastrointestinal bleeding is no longer tenable. Recent advances, coupled with the emergence of a new attitude by some courageous surgeons toward the definitive control of peptic ulcer hemorrhage by a direct surgical attack, call for serious reappraisal." Mortality figures in the 5% range were cited by Crohn in taking a decisive stand favoring aggressive surgical therapy, a position which he has since reiterated as recently as June, 1957.[5] Subsequent demonstrations of favorable results in terms of mortality include the series of Warthin and co-workers,[6] who reported 1 death in 32 emergency or urgent resections (3%); Mathewson and Sugar,[7] who lost 1 patient of 21 operated on during the acute phase of bleeding (4.9%); and a series of 22 consecutive resections for hemorrhage, of which one-half were emergency in nature, performed by Houck,[8] with no mortality.

"Plus Values" in Early Surgical Treatment

However, the question of medical versus surgical treatment remains a controversial one in spite of what seems clear documentation of the wisdom of early resection. We have come to wonder why this should be. On whose side actually is the weight of evidence in the familiar argument between the surgeon who feels that the bleeding should be brought under control by operation and his medical colleague who may consider it necessary to hide the patient away in order to "save him from the surgeon"? This seeming conflict in viewpoint has led us to review our own experience in the matter, especially in terms of end-results, and to philosophize a bit regarding the nature of the controversy.

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We concluded that, in the past, there has been an understandable but seriously misleading tendency to equate medical and surgical mortality figures with total end-results and to overlook thereby certain advantages in gastric resection which we feel are of major importance beyond the primary saving of life.

Between 1953 and 1958 at the Winchester (Va.) Memorial Hospital, 21 patients had emergency gastric resections done by us during the acute phase of bleeding. Two patients died, giving a mortality of 9.5%. The patients were all men, with an average age of 51.7 years. The average preoperative hemoglobin level was 8.5 Gm.%, and the average postoperative hospital stay was 12.4 days. The results were unsatisfactory in four patients; two (group A) died, and two (group B) have had recurrent bleeding since the operation. Results were satisfactory in 17 patients; 1 (group C) required a secondary operation, and 16 (group D) achieved primary good results (see table). In reviewing our material, we noted the application of three general principles: 1. The adoption of a positive course of action is superior, in many respects, to the plan of watchful and hopeful waiting. 2. Patients were provided definitive ulcer treatment. 3. Further improvement in surgical results will derive from earlier performance of operation and improved diagnosis.

Positive Course of Action.—To apprehensive relatives faced suddenly and unexpectedly with family catastrophe and to the physician charged with the responsibility of divining the future in terms of rebleeding, surgical intervention has considerable appeal. It settles the problem quickly and decisively and with mortality prospects proved to be less than those to be expected from conservative management. Smythe and associates[9] commented on the frequency with which patients with hemorrhage obviously potentially fatal come to the hospital, are promptly operated upon, and do well. In our series we have refused surgery to no patient regardless of age, delay factors, or general condition, and have yet to regret the decision to operate.

Summary of Pathology and Results in Twenty-one Patients Having Emergency Gastric Resection*

Case, No.	Age, Yr.	Type of Resection	Date	Pathology, Ulcer	Subsequent Hemorrhage	Result to Date
Group A—Patients Failing to Survive (9.5%)						
1	41	Billroth 1	5/14/56	None found (empiric)	Yes	Continued exsanguination postoperatively; died 15th postoperative day; total of 17,500 cc. whole blood during 29-day illness; extensive esophageal varices and peritonitis at autopsy; no cirrhosis
2	71	Hofmeister	9/27/57	Duodenal (resected)	No	Died 20th postoperative day with bronchopneumonia
Group B—Patients Alive but with Subsequent Hemorrhage Either Unexplained or Uncorrected to Date						
3	66	Billroth 1	9/11/53	Duodenal (resected)	Yes	Readmitted 4/5/54 and 8/24/56 with melena; anastomotic ulcer by x-ray; abdominal vagotomy 8/31/56, with resulting histamine anacidity; readmitted 7/20/58 with melena; x-ray evidence of active anastomotic ulcer; treated conservatively with good result
4	40	Hofmeister	3/12/56	None found (empiric)	Yes	Hematemesis for 4 days postoperatively, requiring 5,000 cc. blood transfusion; readmitted 5/17/56 and 7/23/57 with hematemesis and melena; hiatal hernia by x-ray on last admission; repair advised
Group C—Patients with Subsequent Hemorrhage Corrected						
5	32	Billroth 1	1/15/55	None found (liver normal) (empiric)	Yes	Readmitted 8/12/55; 11/9/56; 11/12/56, with hematemesis and melena; esophagoscopy 11/20/56 revealed esophageal varices; splenorenal shunt 11/22/56; no further bleeding; asymptomatic; drives truck
Group D—Uncomplicated Convalescence, No Further Gastrointestinal Symptoms						
6	48	Billroth 1	8/10/51	Gastric	None	Satisfactory
7	35	Billroth 1	10/ 7/52	Gastric	None	Satisfactory
8	33	Hofmeister	11/ 5/53	Duodenal	None	Satisfactory
9	59	Billroth 1	12/25/53	Duodenal	None	Satisfactory
10	56	Hofmeister	11/11/55	Duodenal	None	Satisfactory
11	61	Hofmeister	1/ 7/56	Duodenal	None	Satisfactory
12	42	Hofmeister	9/ 6/56	Duodenal	None	Satisfactory
13	57	Billroth 1	5/ 7/57	Gastric and duodenal	None	Satisfactory
14	49	Hofmeister	8/19/57	Duodenal	None	Satisfactory
15	46	Billroth 1	8/ 6/57	Empiric	None	Satisfactory
16	51	Hofmeister	2/23/57	Duodenal	None	Satisfactory
17	40	Billroth 1	12/23/57	Empiric	None	Satisfactory
18	58	Billroth 1	12/18/57	Gastric	None	Satisfactory
19	59	Hofmeister	1/21/58	Duodenal	None	Satisfactory
20	72	Hofmeister	7/13/58	Duodenal	None	Satisfactory
21	67	Hofmeister	8/ 9/58	Duodenal	None	Satisfactory

* All patients were men.

Definitive Ulcer Treatment.—Subtotal distal gastric resection, although not a perfect solution, has nevertheless been extensively tested during the past 25 years and has proved a reliable answer to problems of complicated peptic ulceration in 85%-90% of patients operated on.[10] It is of interest that, of the 19 survivors in our series, 17 (including one who required an additional operation before achieving this status) are entirely free of gastric complaints, have had no further bleeding, and face the future with relative certainty in regard to subsequent ulcer formation and/or hemorrhage (see table). This stands in decided contrast to the salvage group of medically treated patients whose future remains clouded by continuing ulcer diatheses with all the problems attendant thereto. According to Crohn,[5] subsequent hemorrhage will occur in from 60% to 74% of the latter group, and it is axiomatic that, when it does, not only will the same anxieties present themselves but the problem will be automatically compounded by advance in age.

Earlier Performance of Operation.—Hoerr, Dunphy, and Gray[3] have emphasized the fact that direct comparison of medical and surgical mortality in the treatment of bleeding of this type is without meaning, since the surgeon in the past has been called on to operate principally on those patients whose bleeding has been either so profound or so prolonged as to create serious doubt as to survival. Among our patients, for example, were one (case 1) who had been hospitalized for 14 days and had received a total of 13,000 cc. of whole blood prior to operation; another (case 5) who had been treated by transfusion with 2,000 cc. of whole blood over a period of nine days; and two others (cases 7 and 8) who had been hospitalized for six days each and had required total blood transfusions of 4,000 cc. and 2,500 cc., respectively, to combat active bleeding. The advantage of earlier intervention in such cases as these is obvious, and it is heartening to note that 9 of the last 11 of our resections have been performed within 30 hours of admission to the hospital.

Improved Diagnosis.—A glance at the table demonstrates that, whereas patients in whom resection is done for gastric or duodenal peptic ulceration achieve almost universally satisfactory results, those who are subjected to resection empirically, anticipated pathology having not been found, attain less satisfactory results. The patients in cases 1 and 5 in our series were subjected to resection because of bleeding subsequently proved to emanate from esophageal varices; these cases illustrate the profound diagnostic problems which can arise in the face of bleeding. Neither of these patients gave a history of alcoholism or hepatitis. One of them (case 1), although showing evidence of esophageal varices on x-ray, showed negative results on esophagoscopy 30 minutes prior to operation. The other (case 5), although eventually found to be bleeding from varices, exhibited negative results on esophagogram and showed, on x-ray, a gastric niche which subsequently proved to be artifact. Finally, further confusing the situation, the liver proved to be normal at operation in both cases. The first patient continued to bleed postoperatively and died 15 days later of exsanguination and peritonitis; the other patient also bled intermittently after operation and was finally placed in the satisfactory group only after splenorenal venous anastomosis was performed 22 months later.

the remaining three patients in whom no
v was discovered at operation and blind
was performed, one (case 4) has bled on two occasions, presumably from a recently discovered hiatus hernia for which repair is planned, and the other two have done well without hemorrhage to the time of writing.

In short, our problems have been more those of diagnosis than technical surgical ones, a situation prevailing in spite of the cooperation of the radiologists who succeeded in pinpointing the lesion responsible for the bleeding in 12 of the 16 cases studied preoperatively. It seems apparent that the greatest opportunity for improvement in end-results lies in the direction of improved diagnosis which will spot the anatomic, resectable lesion and will exclude esophageal varices or other sources of bleeding not benefited by resection.

Clinical Aspects

Age.—The average age of our patients, who were all males, was 51.7 years, the oldest patient being 72 and the youngest 32. Nearly all physicians who write on the subject of gastrointestinal hemorrhage note correlations between (*a*) a decreasing tendency for such hemorrhages to cease spontaneously after middle age and (*b*) an over-all increase in mortality with advance to middle life and beyond. Our own feeling, however, is that the age factor may easily be overstressed if it results in limiting emergency operation to any particular group.

As Martin[10] points out, many instances of uncontrollable hemorrhage occur in the young male, and case 7 in our series would seem to be a case in point. The patient, aged 35, had bled profusely for a period of six days before operation and was found to have a lesser curvature gastric ulcer situated astride and eroding extensively into the left gastric artery. It seems likely indeed that the result would have been fatal had this patient been excluded from operation by any rigid type of age test.

On the other hand, as pointed out by Smythe and co-workers,[6] it is the elderly patient in whom one is most tempted to try the conservative approach that the very factors which make one reluctant to operate also greatly enhance the risk of delay. We feel that age alone should not be decisive in excluding operation.

Surgical Technique.—Once the decision is made, the operation is delayed no longer than is necessary to ensure an adequate supply of blood. The immediate goal is to bring the gastroduodenal bleeding under quick control, and to then give transfusions until the patient's hemoglobin value is at a safe clinical level, after which the operation may be completed in orderly fashion. We have been repeatedly impressed with the similarity between the improvement occurring on the control of the bleeding in these cases and that resulting from the clamping of an offending uterine tube in the case of severe hemorrhage resulting from rupture of an ectopic pregnancy. With the exception of one case, we have relied on rapid devascularization of the greater and lesser curvatures of the stomach and proximal duodenum to produce such control, a procedure requiring from 10 to 15 minutes. In case 17, however, the patient's condition was so critical that it was necessary to manually compress the eroded pancreaticoduodenal artery while hemostatic suture ligatures were placed in the base of the duodenal ulcer before proceeding with resection.

The opinion has been previously expressed by Baker and associates,[11] as well as by Warren and Lanman[2] and others, that exclusion of a duodenal ulcer is a satisfactory procedure provided the duodenum itself is transected and provided the bleeding from the ulcer has been controlled. We have not hesitated to utilize this principle when it appeared helpful, and of the 13 duodenal ulcers in the series 7 were excluded and 6 resected.

Gastrointestinal continuity was reestablished by whichever narrow-stoma technique seemed safest and easiest in the given situation. The Schoemaker modification of the Billroth 1 operation was utilized in 10 instances and the Hofmeister modification of the Billroth 2 in 11.

Length of Operation.—In analyzing 35 patients who had been subjected to either emergency or urgent resection for bleeding, Smythe and his associates[9] found that the mean operating time for the 8 patients who died was two hours longer than that of the 27 survivors. This is an important point, for such patients, as a group, are exceedingly poor operative risks. Even in this enlightened era where premium on speed is properly minimized, it seems obvious that emphasis should be placed on decisive moves which result in control of bleeding, resection of the stomach, and restoration of continuity in a minimum of time consistent with sound surgical principles. The longest time required for operation in our series was 4 hours and 5 minutes, the shortest 1 hour and 50 minutes, and the average 2 hours and 50 minutes.

Empiric Resection.—We have taken the position, along with Gray and others,[12] that, in the absence of demonstrable pathology in the liver, stomach, or small intestine, one should proceed without hesitation to distal subtotal gastric resection. Such empiric resection has the advantage of saving the surgeon from prolonged searching for obscure bleeding sites and allowing him to proceed along a planned course to a conclusion which has proved, on balance, to be productive of good results. Of 20 blind resections performed at the Mayo Clinic and reported by Gray and co-workers,[12a] pathology accounting for the bleeding was discovered in 8 of the resected stomachs when examined in the laboratory.

Complications.—Aside from fatal peritonitis in case 1 and fatal bronchopneumonitis in case 2, major complications were of about average occurrence and included one nonfatal pulmonary embolus, one case of pulmonary atelectasis, one case of partial wound disruption, and a patient in whom the distal esophagus was perforated by the preoperative inflation of the proximal bag of a Patton tube inserted for esophageal tamponade. The right-sided pleural contamination which resulted in this case was easily controlled by a single chest aspiration and the administration of antibiotics.

Comment

Subtotal gastric resection has proved reliable in the treatment of at least 85% of peptic ulcers in which surgery was indicated by the usual complications of perforation, obstruction, history of previous bleeding, or intractability. This generally accepted percentage of permanently satisfactory results can, with propriety, be projected for the relatively smaller group of patients in whom the indication for surgery happens to be the emergency control of massive bleeding. This, to a certain extent, is in the nature of a free dividend on an operation undertaken essentially for the saving of life.

Our attention is attracted, in reviewing these 21 cases, to the 5 patients subjected to exploratory operations with the expectation of finding gastroduodenal ulceration but in whom no pathology was found. The clear indication is for increased emphasis on early and accurate diagnosis. With this object in mind, and borrowing liberally from many excellent articles[13] which document the value of the various procedures employed, we have evolved an intensive diagnostic program designed to bring to bear on a given situation of bleeding all the principal procedures which are helpful in differentiating between hemorrhage from ulcer and that from esophageal varices or other sources. The program is initiated immediately upon admission of the patient to the hospital and is integrated with other laboratory studies such as determination of blood factors and cross-matching for transfusion. It includes (1) routine sulfobromophthalein (Bromsulfalein) retention studies, (2) determination of the blood ammonia level, (3) immediate and uninhibited fluoroscopic examination of the upper gastrointestinal tract with barium, and, whenever indicated, (4) emergency esophagoscopy. The departments of radiology and clinical pathology have been most cooperative in helping to implement this program, and we find that all results can be readily available within three to four hours after admission of the patient to the hospital.

Summary and Conclusions

Twenty-one consecutive patients were subjected to subtotal gastrectomy on an emergency basis for the control of massive upper gastrointestinal hemorrhage in its acute phase. Two patients died, giving a mortality of 9.5%. The fact that the surviving patients were afforded definitive ulcer treatment is of greatest importance and has been insufficiently emphasized in the past. The early and intensive employment of improved diagnostic techniques offers the possibility of real improvement in selecting for operation those patients with hemorrhage who will benefit from resection and in consigning to more appropriate types of therapy those who will not.

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MICROBIAL SENSITIVITY TEST IN MANAGEMENT OF URINARY TRACT INFECTIONS

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Prompt determination of the causative organism and of its sensitiveness to various antibiotics is important in cases of infection. The test here described involves the use of a special culture medium and antibiotic disks. The medium contains whole blood and is spread, with the inoculum, on plates. After incubation, the presence of bright red zones about certain disks indicates the antibiotics to which the predominant organism is sensitive. The method has been applied in a study of 789 specimens from urinary infections, in which the organisms most frequently found were Escherichia, Proteus, and Streptococcus. Patients who had been refractory to prolonged empirical therapy responded quickly, in nearly every case, to therapy based on this testing of the causative organisms.

The extensive use of antibiotics in recent years and the resultant development of antibiotic-resistant strains of micro-organisms have made it increasingly important to determine the drug sensitivity of the causative agent in a bacterial or mycotic infectious process. The more sensitive organisms are killed by low dosages of antibiotics while the resistant strains survive, becoming progressively more resistant.

Moreover, the constantly increasing arsenal of antibiotics and other therapeutic agents available to the physician has placed a demand on the laboratory to provide information about the sensitivity or resistance of organisms to those compounds. The necessity for such information is made more acute by the recognized variations in sensitivity normally inherent in a species and the fact that some strains possess or may develop resistance to those agents in vitro as well as in vivo. Lind and Swanton[1] pointed out that the promiscuous clinical application of specific antibiotics and the general misuse

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of several antibiotics with unsatisfactory results was due in part to the delay by laboratories in providing the physician with information concerning the identity of a micro-organism and its response to one or more antibiotics. From the practical viewpoint, the laboratory can be of definite assistance to the physician in reducing the time required for setting up a therapeutic regimen by reporting the sensitivities even before identifying the micro-organisms.

The method of testing for sensitivity should be reliable, relatively inexpensive, and rapid; when used as a guide to therapy, it is of definite value to the physician and to the patient. The choice of method also seems to influence markedly the results of testing. Jackson and Furland reported a wide range of values when the sensitivity to antibiotics of the same organism was studied by four different methods.

The two methods of testing sensitivity that are now in general use are (1) the "tube dilution method," in which the inhibition of bacterial growth is observed serially in diluted antibiotic broth; and (2) the "disk plate method," originated by Vincent and Vincent,[2] in which the inhibition of bacterial growth on solid mediums is observed around a paper disk containing a known amount of an antibiotic.

Broom and co-workers,[3] with use of disks to determine the sensitivity of micro-organisms, showed that good correlation was obtained with the patient's response to therapy based on these tests. Their results showed the indispensability of sensitivity testing from the clinical standpoint, and demonstrated the practicability of the disk technique in routine diagnosis. Vincent and Vincent[2] and Bondi and co-workers[4] outlined procedures that offered the advantages of simplicity of performance and reduction in the time required for accurate results.

Trafton and Lind,[5] in a study of urinary infections, pointed out that sensitivity testing by the disk method permitted a rapid, accurate, and inexpensive determination of the susceptibility of micro-organisms to the various antibiotics. They suggested that physicians should be encouraged to use these tests routinely and reported clinical data showing that the disk method gave a reliable guide for antibiotic therapy and possible prognosis.

Koch and Bourgeois[6] used disks to determine the resistance of staphylococci and showed that the disk method correlated in every instance with results obtained by the twofold dilution technique. The tube dilution method, because of the time and materials involved, is not suitable for routine diagnostic work and has not offered any advantages over the disk method for clinical procedures.

This new method of determining microbial susceptibility to antibiotics and other therapeutic agents has been adapted by modifying the "base" and "seed layer" techniques, with 15% hemoglobin in the base layer as a color indicator.[7] The oxyhemoglobin in the blood is reduced by the seed layer containing the inoculum of micro-organisms, and the color of the blood changes from bright red to purple. On the other hand, in areas adjacent to the antibiotic disks the metabolic activity of the micro-organisms is destroyed by diffusion, and no changes occur in the blood.

Materials

The materials required for our test include the following inoculum: clinical specimens of urine, preferably catheterized in cases of female patients and second-glass specimens in cases of male patients, spun down for 10 minutes at 2,500 revolutions per minute in sterile centrifuge tubes. The supernatant is discarded and the sediment used as inoculum. Petri plates, 150 mm. in diameter, are covered with a thin layer of the medium and 15% whole citrated blood (base layer, hemoglobin indicator).

The following medium has been developed for rapid sensitivity determination. The medium is highly nutritious and supports and increases the metabolic activity of all pathogenic micro-organisms. It does not inhibit the examination of pathogenic bacteria for sensitivity to various therapeutic agents.

Formula and Preparation of Medium.—The medium used in this test consists of 200 Gm. of beef heart infusion, 150 Gm. of calf brain infusion, 100 Gm. of potato infusion, 10 Gm. of proteose peptone, 5 Gm. of sodium chloride, 2.5 Gm. of disodium phosphate, 10 Gm. of dextrose, and 15 Gm. of agar. Mix calf brains and beef heart muscle, free from fat, with water by stirring and infuse for one hour at room temperature. Heat the infusion to 55 or 60 C and maintain at this temperature for two hours; then filter the infusion through two layers of gauze, pressing as much liquid as possible out of the meat. Heat to boiling; filter through filter paper. Place peeled potatoes in a gauze bag and submerge in water, boiling until soft, approximately 30 minutes. Cool the extract to room temperature and clarify by centrifugation at 35,000 revolutions per minute. Mix this clarified potato extract with brain-heart infusion. Add proteose peptone, sodium chloride, and disodium phosphate; let it dissolve and keep warm at 55 C for one-half hour. Add agar and adjust pH to 7.6. Boil gently in water bath for one hour at 100 C. While boiling add dextrose, a little at a time. Add sufficient distilled water to restore to original volume. Filter through gauze and dispense in screw-capped tubes, approximately 20 cc. in half and 5 cc. in the other half. Autoclave for 15 minutes at 121 C. The final pH should be 7.4. Always adjust the pH with 1% normal sodium hydroxide solution. Store in refrigerator until ready for use.

Antibiotic Disks.—Standardized impregnated disks can be utilized. Two concentrations of each therapeutic agent were used with respect to the

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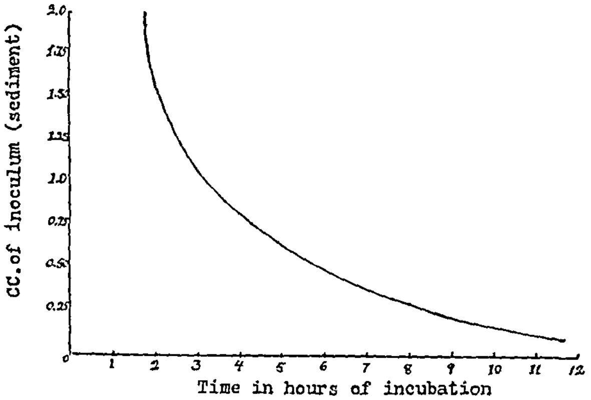

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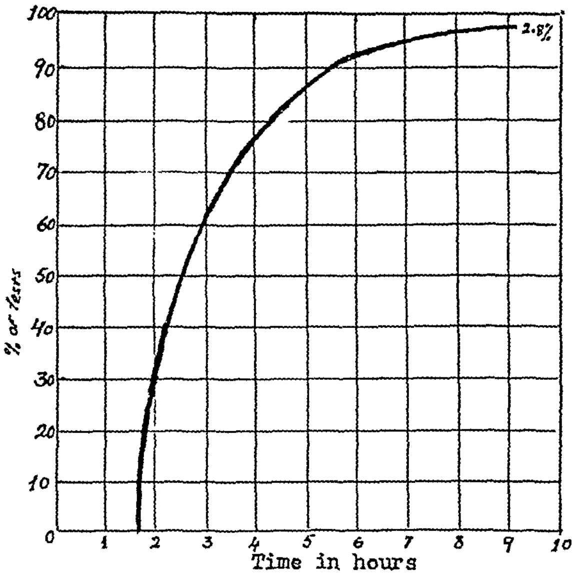

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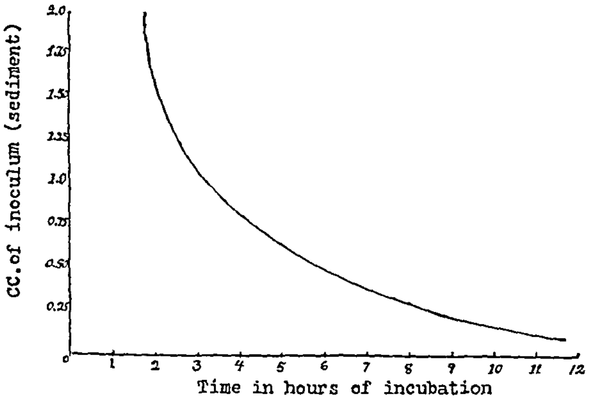

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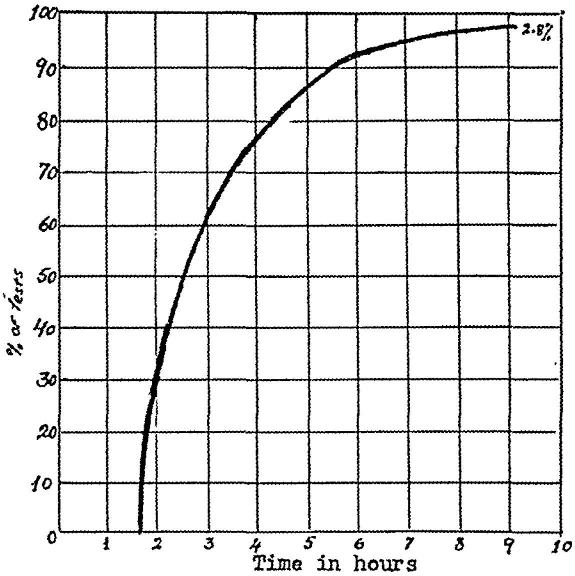

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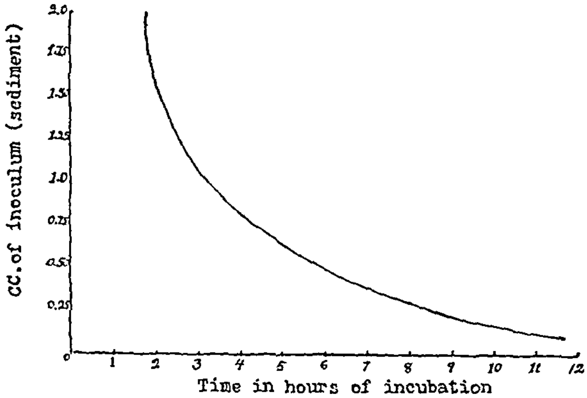

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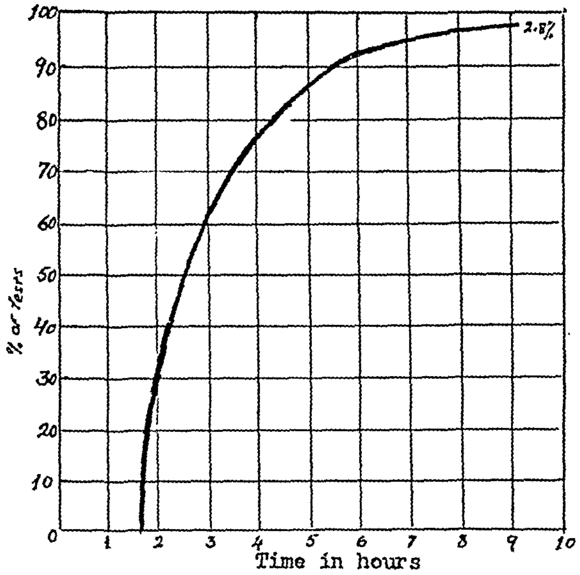

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INCREASING SERIOUSNESS OF RESISTANT URINARY INFECTIONS WITH AEROBACTER AEROGENES

CURRENT EFFECTIVENESS OF KANAMYCIN

John K. Lattimer, M.D., Harry Seneca, M.D., Hans H. Zinsser, M.D.
and
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Urinary infections due to resistant strains of Aerobacter aerogenes are becoming a serious problem in the eastern United States. "Hospital strains" of resistant A. aerogenes have been suspected, similar to the "hospital strains" of staphylococci which are currently causing so much concern across the country. The trend toward increasing numbers of resistant infections with A. aerogenes has been noted only in the time interval since the widespread use of antibiotic therapy, and it has been conjectured that this use has indeed been the cause of the development of more and more resistant strains of this organism.

The clinical data which we have collected here tend to support not only the view that A. aerogenes infections are now more frequent but also that the higher incidence occurs among the patients who have chronic urinary infections rather than acute infections. By experimental means we have attempted to verify the assumption that A. aerogenes has the ability to develop drug resistance more rapidly and more effectively than Escherichia coli. In our experimental laboratory for urologic infec-

Resistant urinary infections with Aerobacter aerogenes were found to be on the increase because of quick mutation to resistant strains. Data were obtained from 20 strains of A. aerogenes and 8 strains of Escherichia coli selected from acutely infected patients. The results showed that the appearance of resistant forms was associated with chronic rather than acute infections. The seriousness of this situation has been reflected in the rising mortality whenever septicemia due to A. aerogenes is encountered. Drug resistance studies led to the speculation that some antibacterial chemical may ultimately hold more promise than antibiotic preparations. Study of biochemical differences in resistant organisms may bring an entirely new approach to the problem of drug resistance. Present practice is to defer any operation or instrumentation of the urinary tract, if A. aerogenes is found to be present, until resistance studies indicate that an effective drug, or combination of drugs, is available in case of trouble.

From the Squier Urological Clinic, Presbyterian Hospital, and Columbia University College of Physicians and Surgeons.

tions, we have documented the interesting ability of A. aerogenes to mutate quickly to highly resistant forms, whereas Esch. coli cannot.

Between 1940 and 1948, Wilhelm and Orkin,[1] in another hospital in New York City, noted an increase from 7 to 49% in the proportion of urinary infections which were due to A. aerogenes. A similar trend in the increase of urinary infections with this organism at the Presbyterian Hospital in New York City [2] has prompted us to study this phenomenon in some detail. It was noted here that the percentage of acute infections of the urinary tract which could be attributed to A. aerogenes was only 14, but that the percentage of chronic infections with A. aerogenes as the causative organism had jumped to 39. The proportion of infections due to other organisms, such as Esch. coli and Proteus vulgaris, remained unchanged when the acute infections were compared with the chronic infections in this group of patients (fig. 1).

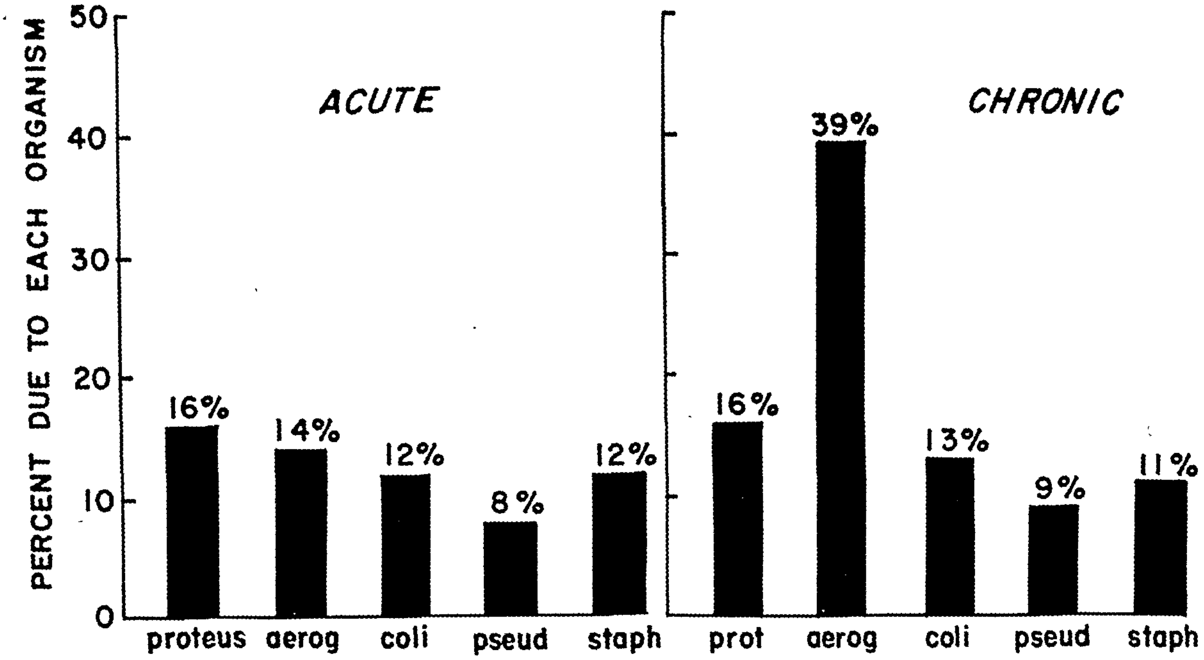

Fig. 1.—Organisms causing urinary infections in hospital in 1958.

It was readily apparent that the increase in numbers of chronic urinary infections due to A. aerogenes was related to the more rapid development of resistant forms by this organism. A trend toward increasing antibiotic resistance among all coliform organisms was noted some years ago by Kirby and co-workers,[3] but the interesting ability of A. aerogenes to develop drug resistance rapidly has been of particular interest to us. The seriousness of this phenomenon has been reflected in the rising mortality whenever septicemia due to A. aerogenes was encountered. In our hospital, during the past five years, the percentage of deaths from septicemia due to A. aerogenes was 60, almost double that from sepsis due to Esch. coli (38%). Within the past two years this has become especially noticeable, with a still sharper rise in deaths due to A. aerogenes septicemia in 1957 (fig. 2). It is notable that in all but 1 of our 10 recent patients with A. aerogenes septicemia the probable origin was in the urinary tract. As a consequence, we have become cautious about operating on patients who have a urinary infection with A. areogenes until bacteriological studies have given us some assurance that we will be able to control any serious infection which may occur during the postoperative period.

Experimental Studies of Drug Resistance

In order to verify our suspicion that A. aerogenes can mutate to resistant forms more rapidly than Esch. coli, 20 strains of A. aerogenes and 8 strains of Esch. coli were selected from our acutely infected patients. These strains were recultured in subinhibitory concentrations of tetracycline, and increasing levels of resistance to tetracycline were thereby induced. It was found that all strains (except one) of Esch. coli did not become more resistant than 25 mcg. per milliliter, no matter how hard we tried. One strain of Esch. coli did achieve resistance as high as 250 mcg. per milliliter but died out quickly on subculture at this level. By comparison, the strains of A. aerogenes rapidly became resistant to high levels of tetracycline, with four of the strains achieving resistance to 850 mcg. per milliliter of tetracycline. All strains of A. aerogenes tested could be artificially induced to quickly achieve levels of resistance in excess of 100 mcg. per milliliter. This put them far beyond the reach of the ordinary therapeutic blood levels achieved with clinical doses of tetracycline. This ability of A. aerogenes to mutate, or change, to resistant forms more rapidly than Esch. coli, in vitro, confirmed our assumption that the rise in chronic clinical infections with A. aerogenes is probably due to this type of phenomenon.

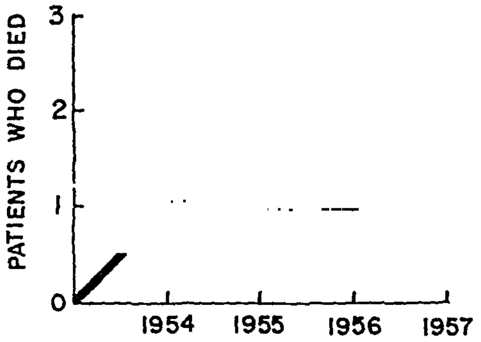

Fig. 2.—Mortality from septicemia due to Aerobacter aerogenes.

To date, medical science has been fortunate in that there has been a continuous parade of new antibiotics and new antibacterial chemicals discovered, many of which are effective, for a time, *against the organisms which have developed resistance* to other drugs. The most recent effective new drug is kanamycin, to which most of our strains of A. aerogenes are currently sensitive. Judging from experience with other drugs, resistance to kanamycin may soon develop, and it will be necessary to discover further antibacterial medications in order to keep this organism under control.

One of our other experiments,[4] not directly related to the A. aerogenes problem, produced some interesting findings in relation to the effectiveness of antibiotic drugs versus antibacterial chemicals. When the drug resistance of strains of Staphylococcus aureus was artificially raised against a number of antibacterial and antibiotic drugs, it was found that *two antibacterial chemicals, namely, nitrofurantoin* and sulfadiazine, were much more effective than the other antibiotic drugs or derivatives which were tested (fig. 3). Extremely high levels of resistance against penicillin, tetracycline, and chloramphenicol could be achieved, but no increase in resistance could be propagated against nitrofurantoin or sulfadiazine. This led us to speculate that some antibacterial chemicals may ultimately hold more promise than antibiotic drugs such as penicillin.

Incidentally, at high levels of drug resistance, cross-resistance against other drugs became apparent. This capacity of highly resistant organisms appeared to us to be interesting and somewhat alarming. It pointed up the necessity for new approaches to the problem of drug resistance.

Whenever organisms were encountered which were completely resistant to all drugs, when tested by the disk method, it was almost always possible to detect partial susceptibility to some drugs if the serial tube dilution technique of drug susceptibility testing was employed. This was of great practical help in selecting proper therapy for highly resistant infections.

Because the ever-necessary search for new antibacterial or antibiotic drugs is likely to encounter the law of diminishing returns, our Squier Clinic experimental bacteriological laboratory is now hard at work endeavoring to determine biochemical differences between resistant forms and sensitive forms of the same organism in the hope that this will lead us to new channels of attack on the problem.

Comment

Resistant urinary infections with A. aerogenes were found to be on the increase because A. areogenes quickly mutated to resistant forms; Esch. coli did not. Resistant forms were found harder to eradicate, and septicemia due to resistant organisms was much more lethal.

Experimentally induced resistance could be pushed much higher against the antibiotic drugs than against certain antibacterial chemicals. The most effective drug for therapeutic use could only be determined by doing susceptibility studies on each new organism encountered. As of 1958, the drugs which were tested for susceptibility with the most chance of success against A. aerogenes were kanamycin, chloramphenicol, novobiocin, sulfadiazine, penicillin, streptomycin, nitrofurantoin, eryth-

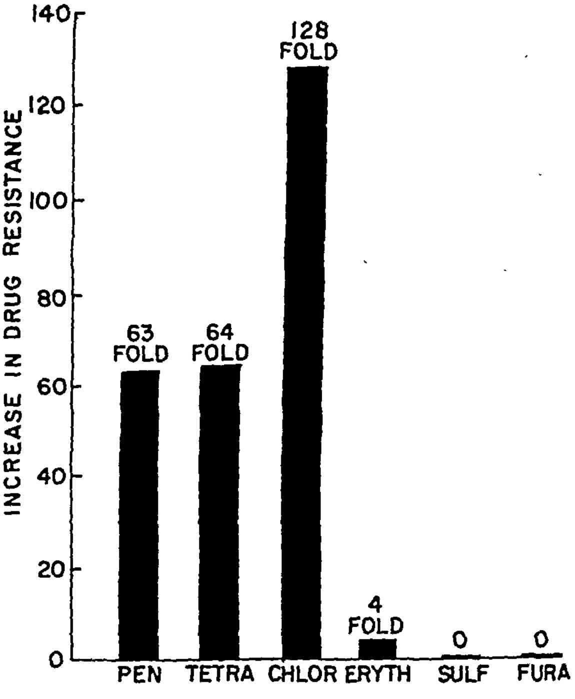

Fig. 3.—Maximum drug resistance which could be artificially induced with penicillin, tetracycline, chloramphenicol, erythromycin, sulfadiazine, and nitrofurantoin.

romycin, and oleandomycin. If the disk method indicated resistance to all drugs, serial tube dilution techniques sometimes revealed partial drug susceptibility at higher drug levels.

The development of cross-resistance at high levels of drug resistance was somewhat alarming, and the never-ending search for new drugs is becoming more difficult. For these reasons we are especially interested in studying the biochemical differences in resistant organisms in the hope of bringing about an entirely new approach to the problem of drug resistance.

620 W. 168th St. (32) (Dr. Lattimer).

This study was supported in part by the Bristol Laboratories, Inc., New York.

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SEVERE HYPOGLYCEMIC SHOCK DUE TO CHLORPROPAMIDE

Lieut. John Robert Coates
and
Capt. Jacob John Robbins, (MC), U. S. Navy

An 88-year-old woman patient had received 250 mg. of chlorpropamide daily for two weeks as a substitute for insulin therapy. When the blood sugar level was found to be 220 mg.%, the dosage was increased to 250 mg. twice daily. After one day, the patient was hospitalized in coma but was released from the emergency room after apparent complete recovery. On the next morning, she was again hospitalized in deep coma and the blood sugar level was 31 mg.%. The next morning it was 8 mg.%. Dramatic recovery was brought about by intravenous administration of dextrose and supplementary feedings. It would appear mandatory that patients receiving chlorpropamide be kept under close clinical observation, with frequent blood sugar level determinations.

Review of the current literature on chlorpropamide (Diabinese), one of the orally given hypoglycemic agents on clinical trial in the treatment of diabetes mellitus, reveals only minor toxic reactions. These include pruritic dermatitis, dizziness, palpitation, drowsiness, nausea, jaundice, and mild hypoglycemia. Although it is recognized that this drug has a slightly greater hypoglycemic effect than other such orally given agents, particularly tolbutamide, no serious hypoglycemic reactions have been reported to our knowledge. Smith and Dube,[1] in a study of 41 diabetic patients receiving chlorpropamide, noted no instances of hypoglycemia. Murray and co-workers[2] reported no instances of hypoglycemia in 43 patients receiving as much as 1 Gm. of the drug daily. In 35 patients receiving 1 Gm. of chlorpropamide daily, Tornow and associates[3] reported hypoglycemic reactions marked by confusion, tachycardia, and hyperhydrosis in 3. The blood sugar levels were never lower than 60, 63, and 67 mg.%. All responded readily to glucose administered orally or intravenously, and, when the dose was reduced, symptoms did not recur. West and McCampbell[4] noted no toxic effects in their study but two patients with symptoms of headache and tremulousness were found to have blood sugar levels lower than 55 mg.%.

It is the purpose of this communication to report the occurrence of severe hypoglycemic shock, prolonged despite treatment over a period of at least 36 hours, with blood sugar levels recorded as low as 8 and 31 mg.% in an 88-year-old patient who had

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received 0.25 Gm. of chlorpropamide daily for two weeks and 0.5 Gm. on the day prior to the onset of deep coma.

Report of a Case

An 88-year-old woman had been under treatment for diabetes by her private physician for a number of years. On a regimen of dietary management and 10 to 15 units of NPH insulin, her condition had been well controlled, with fasting blood sugar levels ranging from 90 to 160 mg.%. There was no prior history of shock or coma. Two weeks before admission chlorpropamide in a dosage of 250 mg. daily was substituted for insulin. On the day before admission, the blood sugar level was found to be 220 mg.% and the dose of the drug was increased to 500 mg. Accordingly, she received 250 mg. in the morning and a similar dose with the evening meal. At about 10 p. m. she retired, complaining of severe headache, weakness, and nausea. Shortly thereafter members of her family found her comatose and totally unresponsive. She was immediately brought to a city hospital emergency room where, after several hours' observation, it was reported that she suddenly sat up, became coherent, and was discharged to go home. According to her family no studies were carried out and no therapy was given.

On the next morning, she again complained of severe headache and weakness and suddenly fainted. On arrival at our hospital at 11 a. m. on Feb. 11, 1959, the patient, an obese, aged woman, was found to be in deep coma, unresponsive to questioning or verbal commands. She reacted to painful stimuli only by faint groans and purposeless motions. The blood pressure was 160/80 mm. Hg, pulse beat 110 per minute, respirations 18 per minute and regular, and temperature 98 F (36.7 C). Motion of all extremities was noted, deep tendon reflexes were hypoactive, and no pathological reflexes were elicited. The pupils were equal in size and responded to light. Funduscopic examination was not remarkable in view of the patient's advanced age. An electrocardiogram was within normal limits. Hemoglobin level was 12 Gm. per 100 cc.; white blood cell count was 8,500 per cubic millimeter with normal differential count; and routine urinalysis was negative for sugar, acetone, and albumin, and microscopic examination showed only occasional granular casts. Blood urea nitrogen level was 21.5 mg.%. The carbon dioxide content was 22 vol.%, but the blood sugar level was 31 mg.%. While intravenous injection of 50 cc. of a 25% dextrose solution was being administered, the patient became responsive and recovered consciousness fully. She was given full liquid diet with supplementary feedings of sweetened orange juice during the day, and a slow intravenous drip of 5% dextrose in water was continued for a period of eight hours.

The next morning she was again found markedly lethargic and could be awakened only with great difficulty. Blood sugar level was found at this time to be 8 mg.%. Repeated estimations on this and newly prepared protein-free filtrates yielded identical values. Intravenous administration of dextrose and supplementary feedings by mouth again produced dramatic recovery. Except for recurring episodes of headache and tremulousness, which responded readily to carbohydrate taken orally, her further course was uneventful. A fasting blood sugar level on the next morning was 111 mg.%.

Careful physical examinations failed to demonstrate evidence of neurological deficit. An oral glucose tolerance test was reported as follows on Feb. 16, 1959: fasting specimen was 119 mg.%; at one hour it was 232; at two hours, 258; at three hours, 265; and at four hours, 200 mg.%.

She was asymptomatic when discharged from the hospital on the fifth day and was again so when seen in the outpatient clinic one week later.

Comment

There is little room for doubt that hypoglycemia was the basis for this patient's coma and that chlorpropamide was the etiological agent. She had received no insulin for at least two weeks prior to admission to the hospital. As stated in the protocol, response to intravenously administered dextrose was instantaneous, and, in fact, results of blood sugar determination were actually received while infusion was being given and recovery had already occurred, so strong was the clinical impression of hypoglycemic shock. Remarkable, indeed, was the finding of further lowering of blood sugar level to 8 mg.% 24 hours after intensive and what was thought to have been adequate treatment by intravenous infusion and oral route. This determination was repeatedly checked by the clinical pathologist on fresh protein-free filtrate. Complete and instantaneous recovery without neurological deficit ruled out cerebrovascular accident, and the patient was at no time hypertensive. The diabetic curve of the oral glucose tolerance test effectively ruled out the possibility of an insulinoma. No other medicaments were being taken by the patient, and a check on the remaining supply of chlorpropamide revealed that there was no reason to believe that dosage greater than that prescribed had been ingested.

Summary

Severe hypoglycemic shock attended by blood sugar levels of 31 and 8 mg.% occurred in a patient receiving the recommended dosage of chlorpropamide. Recurrence of extreme hypoglycemic levels after a period of at least 36 hours, despite intervening liberal administration of carbohydrate, attests to the blood-sugar-lowering potential of this drug. It would appear mandatory that patients receiving

chlorpropamide be kept under close clinical observation and have frequent blood sugar level determinations.

The opinions expressed are those of the authors and not necessarily those of the medical department of the U. S. Navy.

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CLINICAL NOTES

CALCIUM TREATMENT FOR INEFFECTIVE RESPIRATION RESULTING FROM ADMINISTRATION OF NEOMYCIN

W. Philip G. Jones, M.B., Ch.B., Cleveland

Since Pridgeon's[1] description in 1956 of respiratory depression after intraperitoneal administration of neomycin, surgeons and anesthesiologists have become increasingly aware of this problem. Numerous additional reports have since been added to the literature.[2]

Experimental work in animals by Pittinger and Long[3] has shown that neomycin exerts a curare-like action at the myoneural junction so that a complete or partial paralysis ensues. It also has been demonstrated that this neuromuscular blocking action was potentiated by ether and muscle relaxants but could be antagonized by neostigmine and calcium.[4]

Reversal of apnea, by neostigmine therapy, after intraperitoneal administration of neomycin was described in the case report by Middleton and associates.[2e] However, this patient during surgery also received a muscle relaxant, succinylcholine, which may have been responsible for the postoperative respiratory depression. Apnea due to succinylcholine occasionally responds to neostigmine.[5] All the other patients in the cases reviewed were treated by artificial respiration and general supportive measures combined, in some instances, with analeptics.

The following case is believed to be the first reported in which administration of calcium produced reversal of respiratory inefficiency after intraperitoneal administration of neomycin.

Report of a Case

A one-day-old white male in fair condition and weighing 3,075.9 Gm. (6 lb., 13.5 oz.) was scheduled for exploratory laparotomy because of suspected intestinal obstruction. After intravenous injection of 1/600 grain (0.1 mg.) of atropine, anesthesia was induced with 10 mg. of 0.5% sodium pentothal solution and continued with cyclopropane given endotracheally. Respirations were controlled or assisted with a semiclosed technique. Relaxation during surgery was provided by intermittent doses of succinylcholine (total amount 40 mg.), the infant being observed to breathe, move his limbs, and "strain" at intervals throughout the procedure.

Operation revealed atresia of the small intestine requiring excision with side-to-side anastomosis, lasting two and one-half hours. Just prior to peritoneal closure the infant was again moving and breathing spontaneously, and there was rigidity of the abdominal wall. To facilitate closure a further 10-mg. dose of succinylcholine was given. At this time approximately 100 mg. of 0.5% neomycin solution was placed in the peritoneal cavity.

Within 5 minutes extreme flaccidity of the abdomen and limbs was noted, and no spontaneous respiratory movements took place for 30 minutes. When respirations finally resumed they were shallow, ineffectual, and associated with marked tracheal tug together with flaccidity of the limbs. When artificial respiration with oxygen was discontinued, the infant became intensely cyanotic. Transfusion of 65 cc. of whole blood and injection of 70 mg. of caffeine in divided doses produced no obvious improvement.

About three hours after the completion of the operation, the infant's condition was unchanged. Intravenous administration of calcium was suggested, 200 mg. of a 10% solution of calcium gluconate being injected slowly. The effect was dramatic. Within 10 seconds the respirations became deeper, the tracheal tug disappeared, and good color was maintained when the infant breathed room air. Tone returned to the limbs, and spontaneous movements began taking place. Improvement being maintained, the endotracheal tube was removed after 30 minutes, and the infant was returned to his room.

Fellow in the Department of Anesthesiology, The Cleveland Clinic Foundation and The Frank E. Bunts Educational Institute.

Nine days later another laparotomy became necessary for revision of the anastomosis and the making of a jejunostomy. Exactly the same anesthetic technique was used for the three and one-half hour procedure, except that 100 mg. of succinylcholine in intermittent doses was necessary. No neomycin was instilled into the peritoneal cavity. Immediately after closure of the skin the infant was breathing spontaneously, moving his limbs, and maintaining a good color. Extubation was therefore done, and he was returned to the recovery room in good condition. No respiratory difficulties were observed in the postoperative period.

Comment

The necessity for a subsequent operation under comparable conditions enabled a controlled study to be made, the infant acting as his own control. Because of this, the possibility that the respiratory depression after the first operation was due to the anesthetic agents and relaxant used seems unlikely.

The exact mode of action of the calcium gluconate in reversing the respiratory depression is not known. However, the rapidity of the return to effective breathing, together with the experimental work on nerve-muscle preparations,[6] indicates a direct action on the myoneural junction. Observations by Katz[7] demonstrated that the presence of the optimum concentration of calcium at the myoneural junction is essential for the effective release of acetylcholine after stimulation of a motor nerve. This effect is inhibited by magnesium. Unless effective amounts of acetylcholine are released, muscle contraction does not occur.

It seems possible, therefore, that neomycin might act by decreasing the amount of acetylcholine liberated at the myoneural junction, antagonizing the effect of calcium. This theory receives some indirect support from the demonstration by Brazil and Corrado[8] of the similarity between the neuromuscular blockade produced by another antibiotic, streptomycin, and that resulting from magnesium. In both instances this blockade is reversed by the calcium. Slow injection of the calcium is advisable to prevent undesirable cardiovascular effects.

2020 E. 93rd St. (6).

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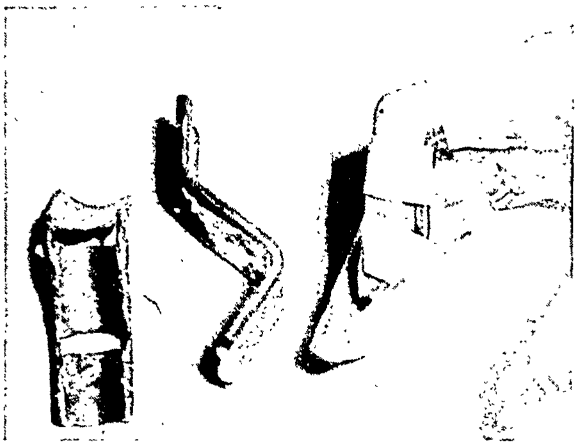
THE ELECTROENCEPHALOGRAM IN EPILEPSY.—The electroencephalogram [EEG] has become an increasingly important tool in evaluating and understanding epilepsy. It has also become quite useful in court cases for the same reasons. Another factor in its popularity in the courts is that electroencephalography is supposedly an objective procedure, something which will be proof of something, and the lawyer—often with a penchant for oversimplification—is prone to look upon the EEG as a definitive authority. This has led to situations where the EEG has been grossly misused and subsequently maligned. The difficulty lies in the lack of specificity in most EEG findings. . . . It is important to make clear in a court of law that the EEG by itself does not usually make a diagnosis, and as physicians well know, it should be used as corroborative evidence interpreted by correlation with clinical data. A history of the patient together with observation of the patient is of far greater value in diagnosing disease than the isolated EEG, which can be quite misleading. This should be especially emphasized and respected in medicolegal cases. Variations of the EEG are found in many clinical states (and in normals); thus "paroxysmal dysrhythmia" and other common findings are an interpretive problem. Commonly EEG's are "compatible" with epilepsy, but not diagnostic. On the one hand, 15 to 20 per cent of normal people who never have had a seizure will show an "abnormality" on the EEG; on the other hand 10 per cent of known epileptics may show no EEG abnormalities.—I. N. Perr, M.D., Epilepsy and The Law, *The Journal of Nervous and Mental Disease,* March, 1959.

NEW SPLINT FOR TREATMENT OF MALLET FINGER

Freeman D. Fowler, Idaho Springs, Colo.



Splint for use in treatment of mallet finger.

Injury caused by forcible flexion of the finger, i. e., mallet finger, has always been difficult to treat. In these injuries there is avulsion of the extensor tendon of the finger without bone injury, avulsion of the tendon with a triangular fragment of bone from the base of the dorsal surface of the phalanx, or, in children, avulsion of the tendon with the whole epiphysis at the base of the phalanx. The results obtained in these cases have been very poor. Plaster used for immobilization comes loose in three to seven days. Dorsal splints with rubber bands going to the distal phalanx should be effective, but patients cannot stand the pressure over the dorsal aspect of the middle phalanx, and they loosen the bands as soon as they leave the office.

Patients with typical flexion deformity at the terminal, which cannot be fully extended, and hyperextension deformity at the proximal interphalangeal joint, which cannot be fully flexed, have therefore shown poor results.[1] In these cases recovery is possible only if the raw bone area on the terminal phalanx is accurately opposed to the retracted extensor tendon. The terminal joint must be held in full hyperextension, and the proximal joint must be held in flexion to overcome the retraction of the extensor tendon.

I have devised a splint of copper wire and copper sheet metal (see figure) which will accomplish the above principles and have used it on several patients, with excellent results. It is inexpensive and can be adjusted to fit the patient's finger. The patient is comfortable while under treatment for the three weeks that he must wear the splint. When waterproof adhesive is used, the splint will not slip off.

1500 Colorado Blvd.

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SENILE KYPHOSIS AND THE KINKED CAROTID.—There appear to be two causal factors in the development of senile kyphosis—degenerative disk disease and loss of muscular tone. With the passage of years, the nucleus pulposus of the disk loses its turgor and the disk becomes desiccated (frequently calcifying in the lower thoracic region), and this results in narrowing of the disk spaces. Narrowing causes bulging of the annulus fibrosus, which strips the periosteum from the opposing vertebral margins, particularly anterolaterally and almost exclusively on the right. Calcification and ossification occur at these sites and give rise to the familiar hypertrophic spur formation. The position of the descending thoracic aorta on the left apparently tends to preclude the formation of osteophytes on the left side. This condition has been termed osteoarthritis or even spondylitis deformans. Since the major changes affect the disks and the vertebral bodies—where there are no joints in the true sense of the word—the term degenerative disk disease more aptly describes the underlying pathologic process. . . . The phenomenon of "kinked carotid" is primarily the result of kyphosis. Those unfamiliar with this condition usually make the erroneous diagnosis of aneurysm of the carotid artery or even of enlarged lymph nodes in this area. This pseudoaneurysm is caused by tortuosity of the carotid artery on the right side and usually occurs in obese, hypertensive, arteriosclerotic women who exhibit kyphosis. If the kyphosis and arteriosclerosis are severe, kinking of the carotid may occur in nonobese subjects. . . . Kyphosis, arteriosclerosis, and a high diaphragm in obese subjects combine to cause relative elevation of the arch of the aorta within the thoracic cage. This results in tortuosity of the right carotid artery in an S-shaped bend or, in some instances, in a complete loop. A pulsating mass may be present in the right side of the neck.—L. C. Doubleday, M.D., Radiological Aspects of Carotid Artery Syndome, *Geriatrics,* April, 1959.

certain important changes in patient care practices and procedures have been effected which can be expected to reduce substantially the possibility of injury and harm to patients. What is probably more important, an increasing number of physicians and others involved in patient care are giving evidence of a growing awareness of the need to prevent injury or harm to patients during the course of medical care and thus to prevent patient grievances, claims, and suits. Although much remains to be done, it has been definitely demonstrated that progress can be made and is being made.

The idea of the joint medicolegal education committee is sound. It is feasible. It can work. It is working right now.

525 E. 68th St.

COUNCIL ON DRUGS

Report to the Council

The Council has authorized publication of the following report. Nonproprietary terminology is used for all drugs that are mentioned; when such terminology is not considered to be generally well known, its initial appearance is supplemented by parenthetic insertion of names known to be applied to commercial preparations.

H. D. Kautz, M.D., *Secretary.*

CURRENT STATUS OF THERAPY IN GLOMERULONEPHRITIS

Lowell A. Rantz, M.D., San Francisco

The term glomerulonephritis is applied to inflammatory diseases of the renal glomeruli. Acute and chronic or latent stages may be recognized clinically and anatomically.

Acute Glomerulonephritis

Acute glomerulonephritis is a disorder associated with the appearance of protein, erythrocytes, leukocytes, and renal tubular epithelial cells in the urine. Red blood cell casts may be present and serve to distinguish the disease sharply from others in which bleeding occurs distal to the glomerulus. The full blown clinical picture is completed by the addition of hypertension, edema, oliguria, azotemia, and, in the more severely ill, cardiac enlargement [illegible] congestive failure. Convulsions oc-

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2. The Committee shall be authorized to consider all medicolegal cases or incidents occurring within the Hospital for the purpose of ascertaining avoidable or preventable factors militating against good patient care, solely for the purpose of recommending procedures for avoiding or preventing the future occurrence of such factors. The use of cases and other material should serve to illustrate the specific purpose of the committee and contribute to the development of an attitude of continuing awareness of the need for the prevention of injury or harm to every patient—on the part of everyone associated with the Hospital.

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SPECIAL ARTICLE

This is the third of three papers presented at the Midyear Conference of the American Hospital Association, Chicago, Feb. 4, 1959. The first and second papers appeared in THE JOURNAL, *June 6 and June 13.*

THE JOINT MEDICOLEGAL EDUCATION COMMITTEE OF THE HOSPITAL

August H. Groeschel, M.D., New York

The problem of professional in-hospital liability varies from state to state and from hospital to hospital due to variations in the law; the attitudes of the people of the community; the organization and operation of hospitals; the attitudes, training, and qualifications of doctors on hospital medical staffs; and other factors. There can be little doubt, however, that hospitals and doctors on hospital medical staffs everywhere are faced with this serious problem.

There also can be little doubt that the problem is increasing in volume, as can be measured by an increasing number of claims and suits against hospitals and doctors in many areas of the United States. (In one large hospital in a metropolitan area, the number of suits brought against the hospital averaged one each month for a period of 10 years up to and including 1957. In 1958, however, the number doubled to an average of two each month.) This increase in volume of claims and suits obviously has brought about an increase in costs connected with the servicing of claims, payment of settlements, defense costs, and the payment of judgments. In many areas of the country, particularly in the rapidly growing metropolitan industrial centers, malpractice insurance premiums are on the rise and doctors and hospitals in increasing numbers are finding it difficult and more expensive to obtain insurance against risks in the area of professional liability.

Studies made in various states have indicated that many factors enter into the causation of this problem. The more important of them have been mentioned by Dr. Sadusk and Mr. Ludlam in THE JOURNAL, June 6 and June 13. We can take some comfort—but not very much—in the fact that, although this specific medicolegal problem is growing, its growth is probably not due to a deterioration in the quality of medical and hospital care. There is abundant evidence to the contrary almost everywhere.

Regardless of the causative factors themselves, several things stand out as completely clear. First, the doctors and the hospitals (and particularly the hospital personnel engaged in the rendering of patient care) must face this problem together. As a matter of fact they have little choice; suits initiated on the grounds of alleged malpractice in the hospital now commonly name as defendants not only the doctor or doctors involved but also the hospital as such—and whatever hospital personnel (including interns, residents, nurses, and technicians) may have been involved in any way in the incident or occurrence which is alleged to have ended in a real or fancied bad medical result.

As an example of this I might mention that I was named as a defendant in one suit brought against our hospital even though I had never seen the patient except in the lobby of the hospital as she was being discharged and then only to answer the patient's question, "What is the hospital going to do about my case and the expense that I have been put to because of my doctor's mistake?"

Second, if the hospitals and doctors are to cope successfully with the problem they not only will have to work together but will have to work constructively to define the causes of incidents leading to injury or harm to patients in the hospital and to take steps to correct deficiencies. They must work to eliminate causes and thus eliminate to the maximum extent possible the incidents which result in injury or harm to the patient.

To do this the hospitals and the doctors will have to first acknowledge that there is a problem and then acknowledge that it will not go away unless they do something about it. This will involve talking about it, and this is the first thing that they both must accept. (In the past every effort has been made to keep such trouble hidden.) Insofar as individual cases and individual doctors, nurses, and other hospital personnel are concerned this is not only understandable but essential for obvious reasons. But procedures and practices which can be corrected so that accidental injury and harm to patients may be avoided—these are something quite different. They can be talked about, and they must be talked about.

It is in this area of prevention that the hospital and the doctors on its medical staff can work together—effectively we on the A. M. A.-A. H. A. Joint Committee believe—to improve the medical and hospital care of the patient and at the same time reduce incidents which lead to injury or harm

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From the Society of New York Hospitals.

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The idea of the joint medicolegal education committee is sound. It is feasible. It can work. It is working right now.

525 E. 68th St.

COUNCIL ON DRUGS

Report to the Council

The Council has authorized publication of the following report. Nonproprietary terminology is used for all drugs that are mentioned; when such terminology is not considered to be generally well known, its initial appearance is supplemented by parenthetic insertion of names known to be applied to commercial preparations.

H. D. Kautz, M.D., *Secretary.*

CURRENT STATUS OF THERAPY IN GLOMERULONEPHRITIS

Lowell A. Rantz, M.D., San Francisco

The term glomerulonephritis is applied to inflammatory diseases of the renal glomeruli. Acute and chronic or latent stages may be recognized clinically and anatomically.

Acute Glomerulonephritis

Acute glomerulonephritis is a disorder associated with the appearance of protein, erythrocytes, leukocytes, and renal tubular epithelial cells in the urine. Red blood cell casts may be present and serve to distinguish the disease sharply from others in which bleeding occurs distal to the glomerulus. The full blown clinical picture is completed by the addition of hypertension, edema, oliguria, azotemia, and, in the more severely ill, cardiac enlargement with or without congestive failure. Convulsions occur in a very few cases.

Nearly all illnesses exhibiting this pattern, and a high proportion of all others in which glomerular bleeding occurs, are the result of group A hemolytic streptococcus infection. Only a few strains of these organisms, notably those of types 4, 12, and 49 (Redlake), are able to produce this disease. The usual sequence of events includes a streptococcic respiratory infection, which may be mild or clinically inapparent, followed by a period in which the individual recovers and seems well. Nephritis develops two to three weeks after the initial illness. A considerable number of cases arise as complications of streptococcic pyoderma.

Glomerulitis may occur in a variety of other conditions including polyarteritis nodosa, disseminated lupus erythematosus, and others of the collagen diseases, in hypersensitivity states and drug reactions, in bacterial endocarditis, and, in certain cases, without a definable precipitating disease. The establishment of an etiological diagnosis is essential for the determination of the prognosis. Poststreptococcic nephritis has a striking tendency to recovery, whereas many of the other types may be expected to have a protracted course. Not infrequently the clinical evidence of a renal lesion will call attention to a generalized disorder that may even lead to death.

Assessment of the prognosis and results of treatment in glomerulonephritis is also complicated by the fact that exacerbations of the chronic form of the disease may be clinically indistinguishable from the acute stage and may also have occurred after a streptococcic infection. In these instances improvement may occur, but complete healing is not to be expected.

Culture of the nasopharynx before any antimicrobial therapy is administered and determination of the serum antistreptolysin 0 titer are essential diagnostic studies in patients with renal bleeding. The isolation of group A streptococci or an antistreptolysin titer of 250 units per milliliter or more increases the probability that the disease is a poststreptococcic nephritis. An antibody level of 100

From the Department of Medicine, Stanford University School of Medicine.

units per milliliter or less excludes this possibility and indicates the need for a careful search for one of the other causes of this syndrome.

Treatment of Poststreptococcic Nephritis

Clinical Course and Prognosis.—A very few patients with poststreptococcic nephritis die within days or weeks of the onset of the disease as the result of acute persistent renal failure. This sequence of events should always suggest another diagnosis such as polyarteritis nodosa or bacterial endocarditis. Continuing subacute activity with a progressive decline in renal function and death within a year characterizes another small group (not over 5% of all cases). Some of these doubtless represent examples of exacerbation of a previously unrecognized chronic nephritis.

About 10% of patients with poststreptococcic nephritis have been said to enter a chronic or latent phase characterized by the presence in the urine of protein and erythrocytes in small amounts and numbers. This phase may persist for years before deterioration of kidney function supervenes. Few serial studies have been made of acute nephritis of proved streptococcic origin. Recent investigation of this disease in young adults suggests that latency is extremely uncommon and that complete healing nearly always occurs.

It has often been stated that the chronic nephritis, which is discovered in persons in whom no history of an acute illness may be obtained, has followed poststreptococcic nephritis that escaped clinical recognition. This point of view may be altered in the future if the frequency of healing of definite streptococcic nephritis proves to be greater than has been supposed.

These considerations require a reevaluation of the prognosis in streptococcic nephritis. It is proper to assume a most optimistic position. Less than 5% of all patients will go rapidly into acute or subacute progressive renal failure, with death in days to months after onset of the disease. Nearly all of the remaining patients will recover, although healing may require one to two years.

Antimicrobial Therapy.—Substantial evidence exists which indicates that persistence of group A streptococci in the tissues of the pharynx is intimately concerned with the pathogenesis of rheumatic fever after a streptococcic respiratory infection. It is now agreed that these organisms should be eradicated by administration of antibiotics when treatment of this disease is instituted. Similar information pertaining to glomerulonephritis is not available, but this procedure is safe and sensible, particularly since the carrier of nephritogenic streptococci is a major health hazard. Even though hemolytic streptococci are not demonstrable in a throat culture, small numbers of these organisms may be present and escape detection. Penicillin is the agent of choice and should be administered in one of three ways: (1) benzathine penicillin G (Bicillin, Permapen), 900,000 to 1,200,000 units intramuscularly as a single dose; (2) buffered potassium penicillin G (Dramcillin, Penalev, Pentids) or phenoxymethyl penicillin (Pen-Vee, V-Cillin), 125 mg. (200,000 units) to 250 mg. (400,000 units) four times daily for two weeks by mouth; or (3) procaine penicillin G (Crysticillin, Depo-Penicillin, Diurnal Penicillin, Lentopen), 300,000 units intramuscularly daily for two weeks.

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Those who are quite ill with edema, hypertension, or cardiac failure should rest quietly in bed until the diuretic phase of recovery has passed. This usually requires only a few days. Hospitalization should be avoided unless the nature of the illness indicates that special therapeutic measures may be required. After this period, both in severe and in mild cases, the patient should be confined to the house and immediate environs and should assume a bed and chair existence, with a minimum of physical activity. This regimen should be maintained until healing has occurred or until it becomes evident that further progress will be slow.

Certain patients still exhibit proteinuria and hematuria one to two months after onset of the disease. Healing in these individuals may require several additional months, but it is not desirable to maintain the degree of rest that has been described throughout this period, nor is it known to be advantageous. A gradual increase of activity in this small group of patients is appropriate. The urine should be examined frequently and a strict regimen reinstituted if a definite increase in hematuria or cylindruria occurs.

Diet.—Restriction of fluids to 700 cc. more than the combined total of urine and vomitus, and of sodium to less than 300 mg. per day, is mandatory in patients with edema and oliguria. During the period when these manifestations of nephritis are present, the diet should be high in carbohydrate and low in protein and potassium. After the diuretic phase has passed, edema is gone, and blood pressure is normal, a regular diet may be resumed and fluids given freely. Reduction of protein in the diet has been stressed by some as an important therapeutic measure in acute nephritis, but evidence that this procedure will promote healing or lessen the frequency of chronicity is lacking. An excessively high-protein intake should be avoided. Approximately 1 Gm. per kilogram of body weight per day is an appropriate amount.

Drug Therapy.—Adrenal corticosteroids (glucocorticoids) do not alter the course of the disease and should not be used. Sedatives may occasionally be necessary to control restlessness and anxiety and, rarely, are used in larger amounts as anticonvulsant agents.

Special Situations

The simple measures described will suffice in most cases of streptococcic nephritis. A small proportion of patients exhibit manifestations of the disease that require special attention.

Severe Oliguria.—Severe and persistent oliguria or anuria must be managed with care, since overhydration may be fatal. Management is precisely like that for any other form of acute renal failure. Fluids should be limited to 700 cc. more than the combined total of urine and vomitus. This entire amount of liquid is best administered intravenously over a 24-hour period as a 20% solution of dextrose injection. The patient should, if possible, be weighed daily on a good scale, and fluid intake should be so adjusted that a little loss of weight occurs each day.

Since hyperkalemia is the most serious complication of prolonged oliguria, frequent measurement of the serum electrolyte levels is necessary. When hyperkalemia appears, an effort should be made to reduce the total body store of potassium by the administration of an ammonium carboxylic ion exchange resin. This should be given by mouth in a daily dose of 50 Gm. (smaller amounts are appropriate for children) suspended in sweetened water. In the presence of vomiting, a 10% suspension may be administered as a retention enema and removed after a few hours.

The use of the artificial kidney, if available, must be considered if diuresis does not begin before azotemia and hyperkalemia become severe, in spite of proper medical management. The indications and techniques for the application of this device are beyond the scope of this review.

Congestive Heart Failure.—Digitalis may be used in the treatment of congestive heart failure during the course of acute nephritis, but diuretics are contraindicated. No special therapy is ordinarily necessary. If symptoms are severe, a phlebotomy may be performed profitably, withdrawing 7 to 10 cc. of blood per kilogram of body weight. Careful restriction of sodium intake from the onset of the illness will minimize the possibility that congestive heart failure will appear.

Convulsions.—A few patients with acute nephritis exhibit severe hypertension and convulsions in spite of careful management and restriction of sodium intake. In the past, magnesium has been given parenterally for the control of the convulsive state and for the reduction of blood pressure under these circumstances. This is a hazardous procedure, since these patients have markedly diminished renal function, and overdosage of magnesium, with serious toxicity, is likely to occur. The intramuscular injection of a combination of hydralazine (Apresoline) hydrochloride (0.10 to 0.15 mg. per kilogram of body weight) and reserpine (Rauloydin, Raurine, Rau-Sed, Reserpine, Reserpoid, Roxinoid, Sandril, Serfin, Serpasil, Serpate, Serpiloid) (0.15 mg. per kilogram of body weight) is an effective nontoxic method for reducing the hypertension of nephritis. The effect on blood pressure occurs within 20 minutes and is long lasting so that only a single injection each day is necessary. Side-effects are rare and consist of mild nausea, faintness, postural hypotension, and moderate tachycardia.

Chronic Nephritis

Chronic or latent glomerulonephritis does not require treatment until hypertension and its complications, or renal failure, appear. Drugs to redu blood pressure must be used with caution in tients with glomerulonephritis so that renal f will not be precipitated or enhanced. These a particularly those that block the sympathet glions, should be reserved for those cases in which rapid deterioration of vision and cardiac or renal function seems to be directly related to the hypertension.

No treatment is known to be of great help when progressive loss of renal function leads to the clinical manifestations of uremia. A low-protein diet and careful attention to the intake of fluids and electrolytes will prolong useful life, but the process is inexorable.

The anemia of chronic renal failure is usually not severe, and its correction by blood transfusion does not often contribute to the well-being of the patient. Furthermore, reactions may occur, particularly if blood is administered on several occasions, and may lead to serious deterioration of renal function. For these reasons, administration of washed red blood cells should be avoided unless the anemia is unusually severe and clearly contributes to some aspects of the patient's illness. The use of whole blood, even under these circumstances, is too hazardous. Blood should never be administered as a "tonic" in an attempt to improve the general state of well-being of the usual patient with chronic nephritis and renal failure.

Nephrotic Syndrome

Several forms of renal disease may be associated with the nephrotic syndrome. It is not certain at the present time whether it is often, if ever, a complication of a chronic poststreptococcic nephritis. The prognosis undoubtedly depends on the pathogenesis of the underlying disturbance of the kidney. The recognition of the various forms and the management of some with adrenal steroids cannot be considered here.

* * *

Report to the Council

The Council has authorized publication of the first paper presented as part of a symposium and panel discussion on the Use and Abuse of Adrenal Steroids, together with introductory comments by the chairman-moderator of the program, Dr. Thomas McPherson Brown. The program, sponsored by the Council with the cooperation of the George Washington University School of Medicine and the Medical Society of the District of Columbia, was held at the Lisner Auditorium of the University in Washington, D. C., on Sept. 25, 1958.

H. D. KAUTZ, M.D., *Secretary.*

THE USE AND ABUSE OF ADRENAL STEROIDS

It is well known that the adrenal steroids can cause a variety of complications, some of which are mild and reversible and others more serious and, at times, irreversible. An awareness that side-effects from various drugs must be anticipated has always been a familiar aspect of medical practice. Most physicians have assumed, quite naturally, that the problems posed by the adrenal steroids are similar to those encountered with other drugs. It is now apparent, however, that the adrenal steroids have created a number of new effects and considerations which have not been experienced in the past.

One of the most important aspects of toxicity from the steroids is interference with the natural defense mechanisms of the body during the period when symptomatic relief may be observed. Complications associated with alterations in the immune mechanism are particularly serious because of their insidious and obscure nature. A reduction in host resistance may mask the spread of infection from a previously controlled but unknown focus. In a similar manner, an unrecognized tendency for the development of peptic ulcers may be stimulated by adrenal steroids, and symptoms usually associated with this complication may be suppressed. Such ulcers can progress to hemorrhage or perforation without warning symptoms which would otherwise suggest their presence. These and other complications such as induced adrenal cortical insufficiency, demineralization of bone and collapse of vertebrae, and the transformation of rheumatoid vasculitis into necrotizing arteritis, with the clinical pattern of the disseminated lupus erythematosus or polyarteritis nodosa, provide additional evidence of the unique nature of the medical problems created by the adrenal steroids. General awareness of these matters has been limited, as evidenced by the widespread use of the adrenal steroids for treatment of relatively minor medical conditions.

STEROID THERAPY IN ENDOCRINE DISORDERS

John E. Howard, M.D., Baltimore

Mine is perhaps the easiest of the subjects on today's program with which to deal. Administration of adrenal steroids to patients with endocrine disorders is almost invariably "replacement" therapy; and, if one adopts a simple philosophy that nature is almost always right, the problem becomes one of imitating nature as closely as one can. In other words, the effort is to provide the organism with the same quantity of steroid hormones which the adrenals could have and would have delivered had their mechanisms been intact. I shall develop my thesis along these lines and later perhaps point out some situations in which this philosophy may perhaps be inadequate or less than optimal.

There is excellent reason for believing that under normal conditions the adrenal glands secrete into the circulation approximately 25 mg. of hydrocortisone each 24 hours, and of aldosterone, the equivalent in desoxycorticosterone acetate of 1 to 2 mg. The derivation of these two approximate figures is based on (1) the quantitative urinary output of degradation products of these compounds in normal persons, (2) comparable outputs in adrenalectomized patients to whom 25 mg. of cortisone and 1 to 2 mg. of desoxycorticosterone acetate have been given, and (3) the excellent state of well-being constantly produced in patients with uncomplicated adrenal insufficiency.

For simplicity and to avoid semantic and mathematical minutiae which would greatly detract from the main issues, I shall outline replacement therapy only in terms of desoxycorticosterone (Cortate, Decortin, Decosterone, Doca, Percorten) acetate and cortisone (Cortisone, Cortogen, Cortone) acetate. So far as I am aware, more recent synthetic corticosteroid compounds have approximately the same potency relative to cortisone when used as replacement therapy as when used as anti-inflammatory agents; i. e., prednisolone (Delta Cortef, Hydeltra, Meticortelone, Paracortol) and prednisone (Deltasone, Deltra, Meticorten, Paracort) per milligram are about five times as potent as hydrocortisone (Cortef, Cortril, Hycortole, Hydrocortone) and cortisone. Certain other still newer compounds have about twice the potency of prednisone, and all have the deleterious side-effects in roughly the same proportions.

Adrenal Cortical Hypofunction (Addison's Disease)

Let us begin with a patient with adrenal cortical hypofunction (Addison's disease), whose adrenals have been rendered functionally inadequate by idiopathic atrophy, tuberculous invasion, cancer, or hemorrhage. As with the diabetic, one usually sees for the first time the patient with adrenal cortical hypofunction severely ill from some complication which has brought his condition acutely to a state of crisis or near crisis. I shall mention this later, but now let us prescribe for the patient who has noted browning of the skin, weakness, a little weight loss, and fall in blood pressure in whom laboratory studies are entirely corroborative and in whom no complications exist. One can at once prescribe 2 mg. of desoxycorticosterone acetate daily intramuscularly and 12.5 mg. of cortisone orally after breakfast and supper, with every confidence that he or she will feel nearly normal within one to two weeks and will soon thereafter have regained the lost weight and strength. So efficacious is this therapy that one may confidently predict to the patient that he will feel as well as ever and be able to carry on all his usual activities; I honestly believe that, given the necessary choice, one would today rather be afflicted with adrenal cortical hypofunction than with diabetes mellitus.

The requirement of 1 to 2 mg. of desoxycorticosterone acetate or some other primarily sodium-retaining corticosteroid such as fludrocortisone (Alflorone, F-Cortef, Florinef) acetate in addition to cortisone seems almost uniformly agreed on. There may be a rare patient with adrenal cortical hypofunction in whom cortisone alone will suffice for optimal therapy, but in the department of medicine at Johns Hopkins University School of Medicine we have not seen such a one. Indeed, the commonest finding among patients who have been treated elsewhere without good results is that replacement therapy has been attempted with cortisone alone. A dose of 50 or even 75 mg. of cortisone has been used each day; the patient has not felt well, and signs and symptoms of hyperadrenocorticism have appeared, perhaps because patients with endocrine deficiencies are notoriously sensitive to the products they lack. Excellent well-being is soon established when small doses of desoxycorticosterone acetate are given and the cortisone is reduced to 12.5 mg. twice daily.

The mechanics of administration of these compounds should be mentioned. For simplicity, cortisone acetate given orally is to be preferred, and, despite the fact that the time of action is supposed to last but six or eight hours, patients have uniformly done well on half a tablet (12.5 mg.) taken after breakfast and supper. Cortisone (or hydrocortisone) acetate given intramuscularly is a cumulative drug, potential hormone being yielded slowly to the circulation but for prolonged periods of time. It is, therefore, useless for quick efficacy; but for stupid or incapacitated patients with adrenal cortical hypofunction, Dr. Segaloff states he has found that single injections of 250 to 300 mg. every two weeks yield satisfactory replacement.

Our patients have uniformly been started on therapy with desoxycorticosterone acetate given intramuscularly, and most of them become so used to a morning injection that they prefer to continue on such a regimen, administering it to themselves.

Associate Professor of Medicine, Johns Hopkins University School of Medicine.

Good results may be obtained with depots of desoxycorticosterone acetate, either by pellet implantation (now largely out of fashion) or by the long-acting compound, desoxycorticosterone (Percorten) trimethylacetate, which may be given once per month intramuscularly in the same dosage that one would have given daily, i. e., 60 mg. if the daily dose had been 2 mg. Good results have also followed the use of a daily oral dose of 0.1 mg. of fludrocortisone acetate which substitutes approximately for the sodium-retaining activity of 2 mg. of desoxycorticosterone acetate. On all these regimens the patient's palate is permitted to regulate his intake of table salt.

Patients with Adrenal Cortical Hypofunction Under Stress

When the normal person is placed under metabolic stress as by infection, broken bone, surgical operation, or the like, he responds by a greater output of adrenal corticosteroids. With a small stress he may double the usual quantity secreted; with a major catastrophe 100 mg. or perhaps more of hydrocortisone will be provided per 24 hours. This increased corticosteroid production seems purposive and useful, for the patient with adrenal cortical hypofunction, when under such stress, goes into adrenal insufficiency unless increased dosage of replacement is provided. The theoretical concept involved is much like that for the person with a mild case of the disease before the days of cortical hormones—he had just enough hormone to keep going, perhaps with added salt, but mild trauma of even a minor surgical procedure or a general anesthetic inevitably resulted in death.

So when the well-regulated patient gets an infection or requires a surgical procedure, one raises the dose of corticosteroid (added sodium-retaining hormone is not necessary) to meet the requirements; in a mild attack of influenza one would give 50 mg. of cortisone acetate daily for the duration of the illness; for a major infection like lobar pneumonia or meningococcus meningitis, 100 mg. per day. In illnesses with vomiting or diarrhea and with surgical procedures, it is well to provide parenteral replacement therapy, recalling always that cortisone acetate given intramuscularly is slowly absorbed; therefore, for quick effectiveness one must use soluble hydrocortisone sodium succinate (Solu-Cortef) given intravenously, in comparable doses and spacing of such dosage as defined for the oral preparations.

Crisis of Adrenal Insufficiency

Acute adrenal insufficiency, so-called crisis, may arise, of course, in the patient with previously unrecognized disease and may also occur in the treated patient who sustains an acute trauma which has deprived him of his usual dosage. Now crisis is seen fairly commonly in patients who have been taking corticosteroids as therapeutic agents (and have consequent adrenal atrophy) and who have suddenly been deprived of their drugs. When insufficiency of any degree has existed for even a few hours, much more hormone is needed to restore normal function than would have been needed to prevent the situation from arising in the first place. This is not unlike the need for huge doses of insulin required to bring certain patients out of diabetic coma. As much as 300 mg. or more of hydrocortisone may be needed in 24 hours until acute manifestations have been controlled, and, with the circulatory collapse which usually accompanies adrenal insufficiency, it is almost always requisite to provide the therapy intravenously, together, of course, with other indicated adjuvant measures such as transfusions to maintain blood volume, saline solution for hydration, and glucose. When the crisis has passed, gradual lowering to maintenance doses of corticosteroid is in order. Current information indicates that the total water deficit is not so great as we previously had thought, and that intercompartmental shifts have made water deficit more apparent than real. Hence, we now no longer use the huge quantities of isotonic sodium chloride solution (10 to 15 liters) that we once did, which were likely to result in overhydration and late appearance of edema.

An example may be cited to stress the speed with which one must act in adrenal crisis. A patient with rheumatoid arthritis had been taking 100 mg. of cortisone per day for two years. She contracted lobar pneumonia, and, with her initial chill, she vomited. This occurred at noon, just after the midday dose of cortisone had been taken. She was hospitalized, and antibiotic therapy was begun within two hours of the chill. In the hustle and bustle of these therapeutic measures, the rheumatoid arthritis and cortisone were forgotten. At 10 p. m., though all had seemed to be going well, the patient suddenly became weak, blood pressure fell to very low levels, pulse rose, and shock was serious. A dosage of 100 mg. of soluble hydrocortisone was given intravenously over the next four hours by the wise physicians, who recognized at once the nature of the problem, and by the next morning all was well again. In all likelihood the patient would have been dead by morning had these measures not been used.

Pituitary Insufficiency

Since the adrenal cortex is dependent on adrenotropic hormone of the pituitary and adrenal atrophy occurs in its absence, the problem of steroid replacement therapy in panhypopituitarism is almost identical with that of primary adrenal insufficiency. However, aldosterone secretion does not seem to be under pituitary control, and under most conditions no sodium-retaining hormone need be given. For corticosteroid therapy, one follows the same principles laid down for the treatment of the patient with adrenal cortical hypofunction.

Adrenal Cortical Hyperfunction (Cushing's Syndrome), Adrenalectomy, and Operations on the Pituitary Gland

When one intends to remove a tumor, or totally or subtotally excise the adrenals for adrenal cortical hyperfunction (Cushing's syndrome), plans must be laid to deal with the temporary or permanent adrenal insufficiency which is bound to follow. Because abdominal difficulties such as distention make it unlikely that the patient can take oral feedings for several days, intramuscularly given depot cortisone acetate is the therapy of choice. To build up the blood level, therefore, to approximate delivery of 100 mg. of cortisone per day to the circulation, 100 mg. is given intramuscularly for two or three days prior to the operation, and this procedure is continued during the period of maximal operative stress—two to four days postoperatively. The dose is then reduced to meet the needs of the particular situation. If total adrenalectomy has been performed, replacement will have to be continued for life, and desoxycorticosterone also must be administered just as to the patient with adrenal cortical hypofunction. However, in those patients who have been adrenalectomized for adrenal cortical hyperfunction, more than the usual replacement dose of corticosteroids is needed and usually for long periods of time. Rarely can one achieve optimal results with less than 50 mg. of cortisone per day. Perhaps the tissues have become accustomed to large doses of circulating hormone during the time of adrenal cortical hyperfunction and now need more than does the normal tissue. With removal of a tumor or after subtotal adrenalectomy, the remaining adrenal tissue usually takes over in a few days or weeks, and desoxycorticosterone is not needed. The tapering of the corticosteroid dosage to such patients is a very delicate procedure and must be done with utmost care. For sometimes after removal of a tumor the atrophic adrenal does not resume function, probably from failure of the pituitary to secrete corticotropin, and the patient will then be dependent on extraneous corticosteroid for life. Permanent adrenal insufficiency also occasionally follows subtotal adrenalectomy when the surgery inadvertently causes necrosis of the remaining adrenal tissue.

A word should be said about corticosteroid therapy in thyroid abnormalities, especially hypothyroidism. If the myxedema has resulted from pituitary disease, there is, of course, likely to be adrenotropic hormone deficiency too, leading to adrenal atrophy. When one gives thyroid hormone to such a patient, the added metabolic burden may make manifest the adrenal inadequacy and provoke an adrenal crisis. Patients have died from this series of events. Even with primary hypothyroidism, i. e., originating in disease of the thyroid and with an intact hypophysis, the adrenals may be functionally inadequate; perhaps they, too, have myxedema as suggested by Dr. Howard Means. In any event, it is a good precaution to provide replacement of corticosteroid to severely myxedematous persons when thyroid therapy is begun. One can find out later by tapering the dose whether it will or will not be permanently needed.

There is a converse to this story, too. We have concluded that corticosteroid therapy to the thyroid-deficient patient is quite dangerous, having now seen three persons develop acute psychopathic disorders within the first few days of normal replacement corticosteroid dosage. It would seem desirable, therefore, to be sure of reasonable levels of thyroid hormone when steroids are to be given.

It should be recalled that degradation of corticosteroids is much slowed in thyroid deficiency, as it is in severe liver disease. The step from hydrocortisone to the tetrahydro form cannot be normally carried out; hence, glucuronidation and excretion are delayed. We observed and reported production of full-blown adrenal cortical hyperfunction in a patient with panhypopituitarism to whom only normal replacement doses of cortisone were given, 25 mg. four times daily, but whose thyroid deficiency was not treated. All symptoms and signs of hyperadrenocorticism disappeared when thyroid was given, despite continuance of the same dose of cortisone.

Summary

In a limited discussion of this kind, one cannot take up all the possible variations which may be met in an individual case. An attempt has been made to outline certain principles which may guide one's actions. These simple principles seem soundly based on theoretical and experimental grounds, and, most important, they have proved to be highly successful in practical use at the bedside. There are those who tell us we have too great a faith in Mother Nature and that we undertreat our patients when we follow the precepts I have outlined. The answer is that it works, and our surgical colleagues tell us that they cannot tell the operative or postoperative course of patients so managed from that of the normal individual under similar circumstances. I would agree, however, in acute situations, to err on the side of too much, rather than too little, and, when there is doubt, give more rather than less replacement therapy.

Since the advent of readily available adrenal steroids, they have been used in an effort to counteract circulatory collapse in all sorts of circumstances. It is true that acute adrenal insufficiency sometimes occurs from adrenal hemorrhage and, judging from histological appearance, may exist in fulminating infections of various types. There is usually no fault to find with administering corticosteroids to such patients in the hope that such adrenal insufficiency is indeed their transient problem. However, let not the availability of corticosteroids and the hope that their administration will be efficacious make us lazy and sloppy clinicians. Usually in such instances postmortem examination has shown the presence of an unsuspected internal hemorrhage, or a silent coronary occlusion, or the like. It must be rare indeed for shock of adrenal origin to arise unsuspected in a patient who has had an accurate case history taken and a thorough physical examination.

MEDICINE AT WORK

- No Magic in Hypnosis
- A. M. A. Grants-in-Aid
- Poetry Amid Research
- Health of People Aloft
- Doctors and Athletes
- The "Spaceside Manner"

Dark Continent

A population of 35,000,000 served by 350 physicians and 35 dentists—this is Nigeria, West Africa, as seen by Dr. W. Wyan Washburn during three months spent last winter at the Baptist Hospital in Ogbomosho.

He writes, "The four big killers are dysentery, malaria, tetanus, and tuberculosis with deficiency diseases and obstetrical complications close behind." But Nigerians are also plagued by leprosy, smallpox, filariasis, kwashiorkor, and hundreds of other ailments.

Now back home in Boiling Springs, N. C., Dr. Washburn reports, "Taboos and superstition still hamper the use of scientific medicine in many ways. In one tribe, the wife is sent away from her husband and people if she fails to have her child in the tenth full moon from her last menstrual period. Woe be to the woman who carries a pregnancy through 11 full moons. . . .

"According to superstition, one [of a set of] twins is a devil or evil spirit, but since no one knows which, both have to be killed. If a baby's mother dies in the first five days, he too must die. He must be evil, else she would not have died.

"There is considerable mental illness," continues Dr. Washburn, a member of the A. M. A. Council on Rural Health. "The African lives in a 'spirit world' much of the time, and when he becomes obsessed with the idea that there is a hex in his life, he is a serious mental case."

He concludes, "The great need for Africa is more of everything—education, doctors, hospitals, technicians, sanitation, teaching, training, and time."

Columbia student Kenneth J. Berkes Jr. (*right*) will use his A. M. A.-awarded nutrition fellowship for a three-month research project under the direction of such men as Dr. Theodore B. Van Itallie (*left*), director of medicine at St. Luke's Hospital in New York City.

Amounts May Be Small, but A. M. A. Grants Do a Big Job

—In Tennessee, a physician needs money to buy more chemicals and equipment for an investigation of the use of grafts in repairing arterial defects.

—A big-city researcher asks a grant for animals and drugs to be used in studying the problem of reducing intracranial pressure resulting from trauma to the head.

—A research team at an eastern college needs extra cash for additional culture mediums and other expendable supplies in a study of staphylococcus infections in hospitals.

These requests for funds—and more than 100 others of a similar nature—were received last year by the A. M. A. Subcommittee on Grants-in-Aid. Applications for similar grants for this year are now being reviewed by the Subcommittee, an arm of the Committee on Research of the Council on Drugs.

The amounts awarded by the A. M. A. are small. None exceeds $500, and many are for less. But the grants have one quality seldom found in those from other sources: they are supplemental. Far from being interested in the original subsidization of research, the Subcommittee seeks to supply the extra dollars that will enhance research already financed by other means.

Although it had only $30,000 to offer last year, the Subcommittee spread it widely among the 112 applicants for aid. Only 24 received the full amount asked for (some asked for less than the $500 maximum), but an equal number were turned away. The remainin

64 received some portion of the amount requested, and none turned it down.

Supplies and Equipment

The Subcommittee's announcement of the availability of funds emphasizes that the grants will be made for clinical and basic medical research, but that they must be supplemental to funds from other sources. No more than two grants are made to the same institution, and they are not to be used for the payment of salaries, services, or overhead. Granted funds are usually spent for drugs, supplies, animals, and equipment.

Major research grants are often tightly subdivided and earmarked for specific purposes, so that the researcher who finds he has forgotten to make provision for a necessary piece of equipment, or for sufficient drugs, may find himself hampered in his efforts. "This is where the A. M. A. likes to be able to step in and make its dollars count heavily by offering supplemental aid," a spokesman for the Subcommittee said.

A. M. A. grants are not made to individual researchers. The money is awarded to the institution in which the study is being made and is used by its business office to pay for purchases made by the investigator. The Subcommittee requires an accounting of the disbursements and the return of any unused balance.

Awards in Nutrition

Another A. M. A. group also channels funds to specialized research efforts. Early this year, the Council on Foods and Nutrition awarded ten $600 grants in the form of fellowships to medical students for the purpose of encouraging research in some phase of clinical nutrition.

Recipients of the fellowships are chosen by the Council on the basis of applications submitted by medical school faculty members who administer the awards. Funds for the program are provided by the Nutrition Foundation, Inc., a group formed in 1941 by food and related manufacturers.

Although this is only the second year the awards have been made, there were 32 applications for grants. Dr. John F. Mueller, professor of medicine at the University of Cincinnati College of Medicine, was the senior investigator for a project recently completed by Robert Poe, recipient of one of the fellowships. Mr. Poe's research was in the relationship of lipemia clearing to coronary artery disease.

Dr. Mueller says: "The project was specially planned for him, but will be continued in our laboratory because of the interesting findings he accumulated. I have no doubt that work such as Mr. Poe did . . . may give many clues to the possible etiology of degenerative vascular disease."

"No one expects these students to produce any world-shaking or Nobel-prize-winning research," says Dr. Mueller, "but on the other hand, it does give them an opportunity to get a taste of what research is all about, and stimulate their interest in it."

Dr. E. M. K. Geiling of Odessa, N. Y., is Chairman of the Subcommittee on Grants-in-Aid of the A. M. A. Committee on Research. Other members are Drs. William Dock of Brooklyn, N. Y., Stuart Mudd of Philadelphia, Torald Sollmann of Cleveland, and Wesley Spink of Minneapolis. Dr. Norman V. DeNosaquo of Chicago is Staff Secretary.

Chairman of the A. M. A. Council on Foods and Nutrition is Dr. Charles S. Davidson of Boston. Other members are Drs. George R. Cowgill of New Haven, Conn.; William J. Darby of Nashville, Tenn.; Grace A. Goldsmith of New Orleans; Wendell H. Griffith of Los Angeles; David B. Hand of Geneva, N. Y.; Robert L. Jackson of Columbia, Mo.; L. A. Maynard of Ithaca, N. Y.; Robert E. Olson of Pittsburgh; Clement A. Smith of Boston; and John B. Youmans of Washington. Philip L. White, Sc.D., of Chicago is Staff Secretary.

A. M. A. Committee on Aviation, which wants to be renamed "Committee on Aero Space Medicine," meets in Los Angeles on April 30. Staff secretary, seated in center beside chairman, speaks into muffling mask of recording device so as not to disturb Committee discussion of agenda item (see story next page).

How A. M. A. Group Works To Safeguard People Aloft

The Committee will have broad, over-all responsibilities in all aspects of civil aviation medicine. The immediate problem and concern of the Committee will be the physical well-being of airmen and the safety of the flying public . . .

When the A. M. A. Board of Trustees created a Committee on Aviation Medicine in June, 1957, there was no sputnik, not a single American jet airliner operating, never a hint of today's elaborate screening effort to place a man in orbit. Now, as an illustration of how the A. M. A. panel has handled its "broad, over-all responsibilities" apace with the times, members at their most recent meeting in Los Angeles on April 30 recommended a name change to Committee on Aero Space Medicine. In its two years of existence the 11-man ommittee, under the chairmanship of Dr. Jan H.
sch of Rochester, Minn., has, among its many
an ried actions:
to br ed the establishment of some mechanism
govern rder out of the conflicting policies of two
this cou al groups concerned with the health of
Civil Air 850,000 civilian airmen. (The post of
eral Aviati on was later established in the Fed-
—Called ency recently created by Congress.)
lance of th rticularly close medical surveil-
civilian flight h and working conditions of
ance passenge f "unforgiving high perform-
scribed as plan g aircraft." These are de-
"perhaps in the fu lled by jet, turbojet, and
Such surveillance njet and rocket" engines.
type of plane, acco ary for a crew of this
cause of its high spee the Committee, "be-
take-off speed, and the its high landing and
land the decision is usu ce committed to
fuel limitations." because of

—Recommended that the to
safety for good health of ai ground
including air traffic controller communic
to the medical profession genera he Committe
believes that when more physicia derstand the
importance of this health factor in turn, are
able to impress it on those who p ey roles in
civil aviation operations, then more o se persons
will be willing to disqualify themsel rom such
roles on medical advice.

—Expressed the need for improved me al par-
ticipation in the investigation of aircraft a dents.
Local coroners (many of whom are not even hysi-
cians) now decide whether autopsies are to be per-
formed on victims of such accidents.

At their recent meeting in Los Angeles, A. M. A. Committee members applauded several proposed amendments to civil air regulations dealing with tighter physical standards for airmen. It was recalled that last fall a pilot who had recently passed a federally prescribed medical examination died of a heart attack as he was preparing to command an airliner trip (see box).

Committee members also decided that there is a need to prepare a guide for all physicians regarding the air transport of their patients. Such a guide will be developed after consultation with the Aero Space Medical Association. Commenting on the need for a guide, a Committee member, Dr. Ludwig Lederer, said, "So many well-meaning physicians tell some of their patients, 'No, don't fly,' when what they really mean to say is, 'Don't travel.' Airline transport is becoming increasingly safe for patients—with improvements in cabin pressurization and with reduction of the travel time."

The A. M. A. Committee, trying to keep one jump ahead of the health problems in today's and tomorrow's jet-space age, does not presume it can come up with all the answers. For there are no pat

Better Health at the Stick

Within six months five airline captains die of natural causes not found in recent physical examinations. . . . The copilot safely lands 62 passengers after the pilot suffers a fatal heart attack over Wisconsin. . . . A number of pilots with diagnosed epilepsy, myocardial infarction, psychoneuroses, and even psychoses continue to fly—with and without proper certification. . . .

Acting on these recent revelations in lay press and clinical reports, the newly established Federal Aviation Agency is now tightening up medical examination requirements for pilots in command of commercial airplanes. Beginning July 1 such pilots over the age of 35 (there are a total of 14,000 airlines captains) will have to "pass" electrocardiographic tests. *This addition to other medical* requirements is aimed at finding heretofore undetected cases of myocardial infarction. The FAA also expects soon to place restrictions on any airline command pilot who has a history of a psy-
episode, who requires a hypoglycemic agent
l of diabetes, or who has any other
of the condition. *In the past, because of*
as strict oles, some of those pilots have
Airlines me ying.
the A. M. A.
(see story), long medical departments
lance of the physica dards which are
ness of commercial and FAA rules.
largely through the efforts o are on
sicians that the FAA was crea ine

Chairman of the Committee on Aviation Medicine of the A. M. A. Council on Industrial Health is Dr. Jan H. Tillisch of Rochester, Minn. Other members are Drs. William F. Ashe of Columbus, Ohio; Victor A. Byrnes, Brig. Gen. USAF, of Washington, D. C.; Oran W. Chenault, Capt., USN, of Washington, D. C.; Herbert F. Fenwick of Chicago; Ashton Graybiel, Capt., USN, of Pensacola, Fla.; George J. Kidera of Chicago; Ludwig G. Lederer of Washington, D. C.; William R. Lovelace of Albuquerque, N. Mex.; L. O. Simenstad of Osceola, Wis.; and M. S. White, Brig. Gen., USAF, of Washington, D. C. Staff Secretary is Dr. B. Dixon Holland of Chicago.

solutions to many puzzlers, such as these:

—At what age should an airlines pilot retire (many above the age of 60 surpass their juniors in proficiency)?

—What is the degree of risk to passengers which should be accepted in returning to the plane's controls a pilot who has recovered from a major impairment?

In the very process of seeking solutions to present and anticipated flight problems, the A. M. A. Committee is pursuing its assigned goal of assuring the "physical well-being of airmen and the safety of the flying public."

Bears, Flickers, and Isolation

Physicians Are Developing A "Spaceside Manner"

Black bears seem to be man's best proxy for experiments in abrupt deceleration relating to space flight. There now is promise of preventing heart attacks in passengers bound for Mars. Isolating an entire community for observation may be a necessary first step to interplanetary travel. Induced hibernation could solve many psychological, sociological, and physiological problems confronting space flight planners.

Those were a few of the points brought out in Los Angeles recently at the 30th annual meeting of the Aero Space Medical Association (renamed from Aviation Medical Association). Speakers also discussed "flicker vertigo" associated with propellers and helicopter rotors, and the elatedly profane diar of an airman in "space isolation." The following
excerpts from papers presented at the ASMA et-
ing April 27-29:

HIBERNATION AND BEARS— uction of

While it is principally in the matter o nefit from
energy that we may expect the greate a problem
the use of hibernation, boredom will

Poetry Amid th ost, Impact . .
d allied re-

Despite almost daily reports of advances in various phases of space medi lowed by Sir
search a few clouds of discontent mar that horizonless cosmos. One cloud he Aero Space
John Cockcroft, chief of Britain's atomic research program. While spea future through
Medical Association meeting in Los Angeles (see story) were predictir States and Russia
expanded research, Sir John was pooh-poohing in Australia: better employed in
"The fantastic amounts—thousands of millions—being spent by th
in trying to put a man into space is not warranted. The money c itute drew a round of
medical and biological research on earth." ic knowledge gained by
And in New York City last month, Merle A. Tuve of the must be inflated by re-
applause when he told a Symposium on Basic Rese scientif ion ortance. Most of our pres-
just operating a huge expedition or big scale ocate 40 to 6 lion dollars a year to support
peated public statements until it appear ng lifetimes, in ade the United States would
ent hoopla about space is certain ding investigators dicated to basic research. The
Tuve suggested that if th unt to about half th sts of one year of our current
individual creative sci xact of the General Electric C any, offered a verse to illustrate
have "a solid p method for budgeting s tific research":
total inves tiply your projects by the words I c t pronounce,
act nd weigh your published papers to the rest half an ounce;
I add a healthy bonus for research that's ally pure
(And if it's also useful, your job will be se re).

I integrate your patent-rate upon a mor hly basis
And I figure what your place in the race to conquer space is;

to men in such a state, nor will there be strife among crew members. Weightlessness will also not affect men secured in this state. A major saving in space and load requirements could be effected by reducing food and oxygen supplies. Aging should occur at only half the normal rate during hibernation. What do we need to know to produce true, deep hibernation in man? First, we must be able to lower body temperature to 10 C [50 F] or below without the occurrence of ventricular fibrillation. Second, we must be able to maintain him for long periods in this condition. And we must be able to arouse the man to a normal condition periodically in order to allow energy levels to be built up. A program aimed at such goals must not lose sight of the fact that the mammalian hibernators have solved these problems.

—Raymond J. Hock, Ph.D., Arctic Aeromedical Laboratory, Ladd Air Force Base, Alaska

Eight American black bears have been utilized in abrupt deceleration studies at the Holloman Air Force Base short track facility. They approximate man's conformation and weight, and stand alone easily on their rear limbs with the head at normal inclination. In the forward facing position with a full harness they have sustained g[ravity] levels with reversible lesions which would be unusually painful and not recommended for human volunteers.

—Capt. James E. Cook and Capt. John D. Moseley, Aeromedical Field Laboratory, New Mexico

a few seconds
ently pulsating red
out

STRESS AND HEAR

Until lately we have been un aeration diac lesions by stress in animals. But now done by stress and release of adrenal h Board to learn how to prevent men from hav ee on in closed capsules orbiting in space. Bot scien- hormone applications had to be done si the if performed one at a time there were no lesions.

—Hans Selye, M.D., University of Montrea

FROM FARM TO SPACE—

I propose the establishment of a small human community which would be isolated yet could be observed—in order to simulate a space mission of long duratio How would such a laboratory experiment be organiz At first it might take the form of a farm. Isolation might later be increased by enclosing the area. When the major problems of maintaining this ecological experimental community in balance have been solved, the next step would logically be that of miniaturization—a shrinking process aimed toward reduction of space an weight to make the system feasible for space travel. A interdisciplinary team utilizing the talents of physicists, chemists, engineers, physiologists, veterinarians, foo technologists, and many other physical and biologic disciples are needed to yield a workable solution.

—Lieut. Col. Albert A. Taylor, D.V.M., Air Research and Development Command, Washington, D. C.

FLICKER VERTIGO—

One helicopter passenger reported that "in the space

. . and *Meaning of Research*

Your scientific stature I weigh upon some scales
Whose final calibration is the company's net-to-sales.

And so I create numbers where there were none before;
And thus have facts and figures and formulae galore—
And these volumes of statistics make the whole thing very clear:
Our research should cost exactly what we've budgeted this year!

The following are additional excerpts from the symposium, which was attended May 14-16 at the Rockefeller Institute by 250 leaders in science, government, education, and industry:

We reject a philosophy that emphasizes more dependence upon a centralized approach and direction. Regimented research would be, for us, catastrophe. . . . We cannot improve science and engineering education without strengthening education of all kinds.

—President Dwight D. Eisenhower

The social sciences, psychology, and psychiatry have suffered particularly by the emphasis on applied research at the expense of basic work and the tendency to hurry results into practice. We are beginning to see that we cannot indefinitely depend on the tree of knowledge to produce the apples which keep the doctor away unless we do something about the health of the tree itself:

—Robert S. Morison, M.D., Rockefeller Foundation

Scientists, when they get into government, are their own worst enemies. When they have control over activities of their colleagues—through the recommending of research grants—they become autocrats of the most difficult kind.

—Lee A. DuBridge, California Institute of Technology

Our so-called "pure scientists" are becoming suburban bourgeois—business-minded—coming to work at the same time every day because they are in car pools. And so their interest centers around car pools and cesspools. We need more researchers who can make the scientist's party toast, "Here's to mathematics—may it never have an application."

—Isidor I. Rabi, Columbia University

! seemed to be enveloped in a violudish mist that thickened and blotted al discernment and produced a panic sensa-

Chai

Tillisc

Willi

nassive, brilliant fire balls were being hurled the A. B-36 tail gunner, seeing the sun through ning propeller blades, had a grand mal conision in the aircraft though he never previously had a zure. Another case involved a pilot serving as an airome officer. While standing on the ramp awaiting ngine shut-down of an incoming C-54, he noted the rays of the setting sun through the revolving propellers and promptly had a grand mal seizure. In both inces, the seizures were reproduced in the laboratory by photic stimulation (flickers).

—Maj. Charles A. Berry, M.D., and
Maj. Herbert K. Eastwood, M.D.
Randolph Air Force Base, Texas

MOTIVATION IN ISOLATION—

Math test finished with three minutes to spare. Gerathewohl said: "Even a genius couldn't do the entire thing in one hour." Pardon me, all to hell. . . . Sharpened the pencils for tomorrow's test. Getting a little anxious to get the hell out of this box. . . . Finished math test and had five minutes to spare. Wait till Gerathewohl sees that. I'll have him calling me "genius"! Ha!

—Diary of Airman D. G. Farrell during week of
isolation, as quoted by Siegfried J.
Gerathewohl, Ph.D., Redstone Arsenal, Ala.

How A. M. A. Works with Other Groups for Health in Sports

What is the value of ultrasound in the treatment of athletic injuries?

How might the modification of rules in certain sports prevent injuries?

Is "making weight," as practiced by some wrestlers and boxers, really dangerous?

When members of the A. M. A. Committee on Injury in Sports met in New York City last month to discuss these and related questions, their words did not ring hollowly in professional isolation. Working with them have been school athletic associations. Backing up their medical opinions were reports from athletic directors, coaches, and athletes. Sitting in with them at the meeting itself was a representative of the National Athletic Trainers Association. All have a common goal: Safeguarding the health of the athlete (see Medicine at Work, The Journal, Oct. 11, 1958).

The following are sample opinions voiced by Committee members at the meeting May 17:

"In the present state of knowledge, there seems to be no particular advantage of ultrasound over present modalities in treating various conditions of athletes. In fact, indiscriminate use without medical diagnosis and prescription holds some dangers to the athlete."

"Wrestlers and boxers who attempt large weight

Left, leaders of Aero Space Medical Association gather after session for meeting of A. M. A. Committee on Aviation Medicine. From left to right are Drs. Oran W. Chenault, ASMA first Vice-president; William Kennard, secretary-treasurer; George Kidera, President-elect; Ludwig Lederer, President, and M. S. White, immediate past-president. They are also members of the A. M. A. Committee with exception of Dr. Kennard, who is former acting director of A. M. A. Washington office. Right, ASMA exhibitor adjusts case displaying pressure suit designed for manned space flight.

A. M. A. Committee on Injury in Sports discusses ultrasound at meeting in New York.

losses within very short periods are endangering their health and perhaps their lives. I treated one athlete who developed acute pancreatitis and nearly died after practically starving himself before weigh-in time, and then consuming 6,000 calories in one sitting before the bout."

"More physicians are needed to assume responsibility for assuring proper care of high school athletes."

"If we can work with the individual football coach at the local level we can show him that changing the rules to prohibit blocking below the knee, for example, will allow him to keep his best men in play without the present fear of injury taking them out. We must work with the people involved. We physicians cannot sit on high and say, 'Thou shalt not.'"

Dr. Allan J. Ryan of Meriden, Conn., is Chairman and Dr. Augustus Thorndike of Cambridge, Mass., is a member of both the ad hoc Committee on Amphetamines and Athletics and the Committee on Injury in Sports. Other members of the first-named Committee are Drs. Henry K. Beecher of Boston and William H. Kessenich of Washington, D. C. Other members of the Committee on Injury in Sports are Drs. Carl E. Badgley of Ann Arbor, Mich.; Harold P. Muller of Berkeley, Calif.; Francis Murphey of Memphis; Owen B. Murphy of Lexington, Ky.; William D. Paul of Iowa City, Iowa; and Thomas B. Quigley of Boston. Fred Hein, Ph.D., of Chicago, is staff secretary of both committees.

Amphetamines and Cooperation

It was two years ago that the A. M. A. Board of Trustees established an ad hoc Committee on Amphetamines and Athletes to resolve, by scientific methods, a widespread controversy over the role of these drugs in sports. At a final meeting in New York City on May 16 the reports of two sets of investigators (published along with an editorial in the May 30 issue of The Journal) were considered by the Committee.

While one study indicated that amphetamine sulfate had an uncertain effect on performance, and the other showed improved performance in approximately 75% of athletes, the Committee immediately recognized there was no real paradox or conflict. Rather, they knew, each report was valid under differing frameworks of research rules relating to dosage, interval between drug administration and athletic performance, number of trials, and statistical sample and analysis.

Members cited the two studies, as well as their own survey on extent of use, in a report to the Board. The total report represents the first A. M. A. portrayal of the role of amphetamines in athletics—in fact, the first such specific analysis of its kind in the world. In describing the survey phase, Dr. Allan J. Ryan, Chairman of the Committee, said, "It could not have been presented without the help of coaches, trainers, athletic directors, and team physicians in 734 colleges and 815 high schools—as well as officials of the National Collegiate Athletic Association, the National Association for Intercollegiate Athletics, and the National Federation of State High School Athletic Associations."

Corporations, Too, Help Support Medical Education

What motivated the railroads of this nation to give more than $34,000 last year toward the support of medical schools? Why did the iron and steel industry contribute nearly $137,000, the legal profession $4,700, the automobile makers $159,000, and the entertainment industry over $10,000? How does the American business community or, for that matter, any area outside of this profession, identify its stake in so seemingly remote a field as medical education?

Perhaps it is not remote at all. In its decade of existence the National Fund for Medical Education has disbursed to medical schools nearly 19 million dollars (including 5 million dollars in AMEF funds), contributed largely by companies representing scores of industries. In praising this corporate support, S. Sloan Colt, president of the Fund, reported last month, "Their action reflects industry's concern with both the immediate need for doctors, medical research, and health services, and the long-range need to develop the full potential of the medical sciences. Corporation directors are realizing more and more that medical education is a focal point of national strength."

The NFME was organized by the Association of American Medical Colleges, the American Medical Association, and a group of university presidents headed by Dwight D. Eisenhower, then president of Columbia. The bulk of the $2,046,399 donated to the Fund last year by nearly 2,000 business and professional organizations went to medical schools "with no strings attached." Special-purpose grants supported 15 separate projects aimed at such educational goals as improved audiovisual teaching, interrelation of religion and medicine, and a reduction in the time required to complete an M.D. degree.

Assembling in Chicago for an annual meeting on May 12 representatives of the Fund awarded a joint citation to Theodore V. Houser, retired board chairman of Sears Roebuck and Company. He has long been identified with progress in medical education support efforts and, through the Sears Roebuck Foundation, with improved distribution of medical care facilities. Houser noted that the current contribution by industry only begins to solve the problem of medical schools support. He said, "The real need is a minimum of 10 million dollars a year."

Underlining cooperative efforts in such a gigantic task of support, Dr. F. J. L. Blasingame, Executive Vice-president of the A. M. A., told the assembled physicians and laymen: "The contributions of physicians to medical schools through our American Medical Education Foundation and through individual medical school alumni funds have been multimillion in the past few years. The medical profession's success has been due in part to the sound backing given to medical education by corporations and by individuals."

Taking the Magic Out Of Medical Hypnosis

Ever since last June, when the House of Delegates developed a statement on the medical use of hypnosis, drum-beaters for short-term, high-cost instructional courses have been promoting their hocus-pocus pitch more and more intensively. Now, as a result of its first meeting recently, the new A. M. A. Committee on Hypnosis has begun laying out a program to take the magic out of medical hypnosis: Members hope to outline, within a few months, a suggested curriculum for the teaching of hypnosis at medical-school and postgraduate levels.

While such a course has not yet been delineated, Committee members at their April 25 meeting in Philadelphia expressed the opinion that a proper curriculum approach should:

—Emphasize psychodynamics rather than technique. This stress on the motivational basis of human behavior recognizes the value of long-term perspective in doctor-patient relationships—a vital point lacking in "quickie" hypnosis courses.

Devices and Drama

In the task of pursuing its straight-line goal (see story) the A. M. A. Committee on Hypnosis has had to examine the chaff along with the wheat of activities surrounding this topic. Among items recently called to Committee attention are these:

—A camera-like device (priced at $247.50) which, it is claimed, automatically puts people into a deep trance by means of a soft ticking sound and a blinking light.

—Inquiries from several hospitals regarding delivery room and operating room privileges to nonphysician hypnotists.

—A move by one state medical society against a lay hypnotist for alleged violation of the medical practices act, and the investigation of a hypnosis institute by county prosecutors in another state.

—A one-hour television drama, presented last month, which featured medical hypnosis. (The script was produced with the advice of two A. M. A. Committee members and was reviewed by another A. M. A. Committee which specializes in medical script counsel. See Medicine at Work, The Journal, May 4, 1957.)

—Build an understanding of both immediate and eventual hazards in posthypnotic suggestion and in self-hypnosis when practiced by either the patient or the physician.

—Point up the damage which the entire profession can suffer if hypnosis is used to enhance a medical practice through hints of "mystery," panacea, or "miracle" results.

—Identify hypnosis as merely an adjunctive technique, and acknowledge that many other kinds of approach could be better in selected cases.

—Caution against hypnotizing persons who may have been under treatment for a psychiatric disorder which might be aggravated as the result of a trance.

Commenting on the awareness with which a number of medical educators approach this complex problem Dr. Harold Rosen, chairman of the A. M. A. Committee, said, "In contrast to those sensationalizing brief courses in scattered parts of the country it is refreshing to note that several medical schools are either planning or instituting principles of hypnosis as a part of established curriculums on a reasoned, long-term and integrated basis."

Cruises, Race Tracks and Secrets

Promotional mailings which sensationalize "quickie" courses have been sent to thousands of medical and dental practitioners in recent months—under the sponsorship of physicians, "licensed hypnotherapists," psychologists, private schools, "hypnotists to the medical profession," and even county medical societies. These have carried such labels as "seminar," "institute," "training program," "complete three-day postgraduate course," and "Kentucky Derby Special" (which, according to the literature, includes two reserved seats to the race "and two Gen - u - wine Kentucky Mint Juleps"). Prices have ranged from $85 for a one-day course to $1,195 for an "18-day International Caribbean Cruise Course in Hypnosis." No price was listed for an "April in Paris Hypnosis Course."

The tempo and intensity of such promotion is a source of concern to the A. M. A. Committee, whose members are intent on communicating to their colleagues the values of medical hypnosis while charting the pitfalls of its misuse and abuse. So often, they know, disappointments from inflated anticipation come too late for remedy. One example occurred in 1950 when the seventh-place St. Louis Browns hired a "psychologist hypnotist" to eliminate self-doubts acquired by the team's consistent losers. His contention was that the coordination of these players was destroyed by "fear thoughts to the muscles."

How did the Browns fare after hypnotic effort? They still were seventh when the season closed.

An in-depth report on medical hypnosis is scheduled for early publication in Medicine at Work.

Members of A. M. A. Committee on Hypnosis, under Council on Mental Health, hold their first meeting in Philadelphia, continuing discussions at dinner with benefit of stenotypist and tape recorder. Clockwise from left are Drs. Richard J. Plunkett, staff secretary; M. Ralph Kaufman of New York City; Zigmond M. Lebensohn of Washington, D. C.; Louis J. West of Oklahoma City; and Harold Rosen of Baltimore, chairman.

New Echoes of Danger In Plastic Bags Alert

AT LEAST THREE CHILDREN HAVE SUFFOCATED SO FAR THIS WEEK WHILE PLAYING WITH PLASTIC BAGS IN INDIANA, PENNSYLVANIA AND CALIFORNIA . . .

A wire service news report which included that sentence has accented a nationwide awareness of the peril of discarded plastic garment bags used as playthings. It was six months ago that a Phoenix physician linked the suffocation deaths of four infants to plastic bags with which each had been playing. He notified the A. M. A. Committee on Toxicology and the word was spread to regional health officials. Soon, thanks to the help of local newspapers, individuals in their communities were being warned of the danger.

On April 25, The Journal reported on the joint efforts of medicine and the press to sound the alarm. Then, last month, communications mediums on a broad scale were able to portray a fuller picture from the *United Press International* wire service report. As that story was ticking off May 13 on teletypes in the offices of nearly 2,000 newspapers, magazines, and broadcasting stations, these things were taking place:

—The National Safety Council was estimating that 100 small children might be suffocated in plastic bags this year.

—The plastics industry was organizing wide distribution of a pamphlet warning against reuse and abuse of the packaging material.

—The Public Health Service was reviewing recent and past infant deaths to determine action on its part.

—A Chicago dry-cleaning chain was discontinuing use of $2,500 worth of plastic bags, and an Indianapolis dry cleaner was stencilling his bags with the warning: "Danger. Keep away from infants. Danger of Suffocation."

—Legislation was being prepared in Congress and several states, dealing with perforation or labeling of the bags.

The alert remains alive. It shows the accomplishments of cooperative effort when the medical profession and communications mediums pursue a common public service goal quickly, factually, and unselfishly.

MEDICINE AT WORK in future issues

- ***Fire Rescue Squads***
- ***Interlingual Doctors***
- ***Planning Tomorrow's Hospital***
- ***Radiation—Double-Edged Sword***
- ***Local Teamwork in Aging Program***

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MEDICOLEGAL ASPECTS OF HEAD INJURIES

MANY cases of head injuries have medicolegal aspects. Persons who have sustained head injuries as the result of an occupational injury or through someone's negligent act sometimes seek recovery of a monetary award in a civil suit or compensation hearing. Awards in such proceedings often include money damages for factors not directly related to earning capacity, namely, mental distress, pain, disfigurement, and personal grievances, and require of the physician an emphasis on certain aspects which are not always well documented in routine medical practice.

The prime consideration of the physician when he sees a patient with a head injury, of course, is to determine precisely the severity of brain damage, if any, and to treat it as best he can. An accurate assessment of such damage, according to Walker,[1] depends on data dealing with evidence of external violence, proof of impairment of mental functions, and neurological deficits or abnormalities as found in certain types of laboratory examinations.

Fractures visible in roentgenograms of the skull indicate that the head was subjected to at least a certain degree of violence, but the severity of a head injury is not necessarily correlated with the extent of the skull fracture. Severe neurological disturbances may follow injuries that cause very minor fissures in the skull or no fractures whatever. Examination of the cerebrospinal fluid several hours after a head injury may reveal blood in the fluid; ordinarily, this provides evidence of head injury, provided a ruptured aneurysm is ruled out. The amount of blood in the cerebrospinal fluid is not, however, an index of the severity of the injury, for the fluid may be virtually clear in cases of severe head injuries and quite bloody in relatively minor head injuries.

An electroencephalogram made shortly after a head injury may demonstrate alterations in brain waves. Since about 15% of the general populace have some degree of electroencephalographic abnormality, a single electroencephalogram should not be considered proof that the brain was injured, because it is difficult to be sure that a single electroencephalogram taken before the injury would not also have been abnormal. However, if repeated electroencephalograms of a patient who has sustained a head injury made over a period of several weeks demonstrate reversal of the alterations of brain waves to a normal pattern, it is justifiable to conclude that damage to the brain produced the initial change in the electroencephalogram.

It is often mistakenly assumed that brain injury will necessarily lead to permanent mental or neurological impairment. Minor injuries and sometimes major injuries frequently do not cause the slightest demonstrable impairment of mental or nervous function. While it is probably true that a blow to the head which results in unconsciousness for more than an hour or two indicates organic damage to the brain that will not be repaired by nonneural functioning tissue, it does not follow that such an injury will permanently impair cerebral function. In general, the ill-effects of most head injuries pass off within six months; some patients, however, have persistent symptoms, neurological sequelae, or paroxysmal attacks of unconsciousness to mar their return to good health.

Most patients whose head injuries are sufficient to impair consciousness experience symptoms of headache, dizziness, amnesia, mental confusion, and nervousness for short periods of time, usually for a few weeks, although they occasionally persist or recur for longer periods. In a small percentage of patients who exhibit persistent symptoms, these form a consistent clinical pattern so that they have been called the post-traumatic or post-concussional state or syndrome. Patients thus affected complain of headache, dizziness aggravated by postural changes, insomnia, tinnitus, difficulty in concentration, memory impairment, nervousness, visual disturbances, and anxiety. Whether the post-traumatic syndrome is due to organic brain damage or to neurosis has been argued for generations. In evaluating persons who have had this syndrome for a year or two after injury, it is advisable to consider the findings obtained from neurological examination, roentgenograms of the skull, electroencephalograms, psychometric testing, and, in some instances, psychiatric examination. Evaluation of the clinical symptoms of the post-traumatic state requires knowledge of the patient's intelligence and personality as well as of any neurological deficits and evidence of convulsive manifestations. Presence of any of these sequelae does not necessarily mean that the patient will be permanently disabled, for these sequelae tend to regress spontaneously with time and with resolution of litigation.

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[1] Walker, A. E.: Medicolegal Aspects of Head Injuries, Postgrad. Med. 24:A-34-A-46 (July) 1958.

The medicolegal evaluation of a disability due to an impairment caused by a head injury is somewhat more complicated, difficult, and uncertain than the evaluation of a disability due to an impairment caused by a leg, arm, or eye injury. The latter yields more readily to measurement. Fortunately, however, the physician is not required to place a monetary value on either impairment or disability, although the patient's attorney must do so and would, no doubt, like the physician to do so. Perhaps some of today's excessive verdicts could be avoided, some liability insurance premiums reduced, and the over-all administration of justice improved if more emphasis were placed on the maximal medical rehabilitation of the patient and less on the assessment of a monetary reward for injury.

DR. E. VINCENT ASKEY—PRESIDENT-ELECT

At the 108th Annual Meeting of the American Medical Association in Atlantic City the House of Delegates named Dr. E. Vincent Askey, prominent Los Angeles surgeon, the new President-Elect. He will take office as 114th president in June, 1960, at the Miami Beach meeting. Dr. Askey was elected by unanimous vote of the House of Delegates which first elected him their vice-speaker in 1952, and their speaker in 1955.

Dr. Askey was born in Sligo, Pa., Aug. 15, 1895. He received a bachelor of science degree in 1917 from Allegheny College and his medical degree in 1921 from the University of Pennsylvania. He spent his internship and residency, respectively, at the Hospital of the Protestant Episcopal Church and Kensington Hospital for Women in Philadelphia. Dr. Askey's brother was severely wounded at St. Mihiel in World War I, and spent his last days in Los Angeles. It was his brother's serious condition that took Dr. Askey, as a young surgeon, to California. In 1948 he was certified by the American Board of Surgery, and later he became a fellow of the American College of Surgeons. He is on the surgical staff of St. Vincent's Hospital in Los Angeles.

E. Vincent Askey, M.D.
President-Elect of the American Medical Association

He was especially honored in June, 1958, when he was called back to Allegheny College at Meadville to receive the honorary degree of doctor of science. Despite a busy practice, the citation said, Dr. Askey had found time to serve as a member and president of the Los Angeles City Board of Education, combining high ideals, responsible citizenship, and distinguished professional achievements. His sponsor at the ceremonies was the professor who had first introduced him to biology 45 years earlier.

In 1943 Dr. Askey served as president of the Los Angeles County Medical Society and in 1948 as president of the California State Medical Association. He is a member of Alpha Omega Alpha, Nu Sigma Nu, Delta Tau Delta, and Alpha Chi Sigma. He is married to the former Martha Nebinger, whose ancestors boasted five consecutive generations of physicians. The Askeys have two sons, Edwin Vincent Jr., and David Harrison, a premedical student in Colorado, and a daughter, Jane. They also have four grandchildren.

DR. DE BAKEY GIVEN DISTINGUISHED SERVICE AWARD

Dr. Michael E. De Bakey of Houston, Texas, chairman of the department of surgery at Baylor University College of Medicine, was chosen to receive the American Medical Association's Distinguished Service medal on June 8 at the annual meeting in Atlantic City. The many names submitted to the Board of Trustees were screened and the three they selected were voted on by the House of

Delegates. The gold medal, one of medicine's highest awards, was bestowed on Dr. De Bakey at the inaugural ceremonies on June 9.

Dr. De Bakey is a graduate of Tulane University School of Medicine in New Orleans, where he taught for many years. He has made many contributions to the advance of heart and blood vessel surgery, including the development of the milking-action pump which has been widely used in heart-lung machines. He has been a member of the Council on Scientific Assembly of the American Medical Association since 1950, and is widely known particularly for his work in the use of artery grafts and plastic substitutes as replacements for diseased portions of arteries. In 1954, he received the Matas award for his work in vascular surgery. During World War II, he served as the director of the surgical consultants division in the office of the Army surgeon general, with the rank of colonel. In 1946, he was awarded the Legion of Merit.

Former president of the Society of Vascular Surgery and the Southwestern Surgical Congress, Dr. De Bakey is a member of numerous scientific associations. One of his most recent appointments was to membership on the National Advisory Heart Council. In this capacity, he makes recommendations to the surgeon general of the Public Health Service on programs of the National Heart Institute. The council reviews requests from nonfederal institutions and individuals for research and teaching grants in the field of diseases of the heart and circulation. Dr. De Bakey and his surgical associates at Baylor have in the last seven years installed hundreds of arterial grafts. More than 500 have been for aortic aneurysms alone. Another 500 or more have been for occlusions of the aorta or of the lesser vessels. Other grafts which he and his team have installed were used to correct congenital constrictions of the aorta.

MICHAEL E. DE BAKEY, M.D.
AWARDED DISTINGUISHED SERVICE MEDAL

EXERCISING AND VIBRATING MACHINES

The seizure by the Food and Drug Administration of vibratory appliances recently promoted and advertised as weight reducers and as cure-alls for disease is a significant step.[1] Approximately every generation since the middle of the 19th century has seen exercising and vibrating machines manufactured and sold for alleviation of disease.

About 1857, Dr. Gustaf Zander of Stockholm first used mechanical equipment for massage and exercise. Several large hospitals in the United States were thereafter equipped with "Zander rooms."[2] Machines of all styles and shapes were belt-driven and designed to imitate mechanically many motions normally performed actively by human beings, such as bicycling, rowing, and arm, leg, neck, and back exercises. The Zander machines enjoyed several years of popularity and then fell into disuse in view of the lack of evidence to support their therapeutic claims.

Massaging, exercising, and vibrating machines were revived in the 1920's and sold by the thousands with claims that they reduce weight and prevent or cure arthritis, bursitis, stroke, multiple sclerosis, or heart trouble. Some of these early machines were advertised to relieve backache, headache, menstrual cramps, and nervous tension.

Some medical organizations then as well as at present have permitted promoters and distributors of these devices to exhibit and demonstrate at medical meetings, at both the state and the national level. This implication of approval is unfortunate since it does not represent the thinking of scientific medicine.

The 1950 crop of massaging, vibrating, and exercising machines proved to be no more or less effective than the Zander machines of a century previous. In its release, the Food and Drug Administration wrote that the machines "may be soothing and relaxing to the user and help to relieve minor aches and pains due to fatigue or over-exertion. They should not be represented as effective for treating disease or weight reduction."[3] In most instances, the FDA has obtained relabeling of the devices with unwarranted claims eliminated. Physicians might well call the attention of their patients to the report of the FDA and continue prescribing rational treatment for obesity by diet, active exercise, and drugs.

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1. Cure-All Devices Seized by FDA, A. M. A. News 1:6 (Oct. 20) 1958.
2. Krusen, F. H.: Physical Medicine, Philadelphia, W. B. Saunders Company, 1941, p. 524.
3. September Report, U. S. Department of Health, Education, and Welfare, Food and Drug Administration, 1958.

ORGANIZATION SECTION

STANDARD NOMENCLATURE COMMITTEE CHAIRMEN

Following is a list of the Standard Nomenclature Committee chairmen. Those who wish to make suggestions relative to Standard Nomenclature of Diseases and Operations entities should contact the respective chairmen before June 30, 1960.

ANESTHESIOLOGY
Huberta M. Livingstone, M.D.
5805 Dorchester Ave.
Chicago 37.
BACTERIOLOGY
William Burrows, M.D.
Department of Bacteriology and Parasitology
University of Chicago
5724 Ellis Ave.
Chicago 37.
BODY AS A WHOLE
Paul S. Rhoads, M.D.
720 N. Michigan Ave.
Chicago.
DENTISTRY
Harold Hayes, D.D.S.
2376 E. 71st St.
Chicago 49.
DIGESTIVE
Burrill B. Crohn, M.D.
1000 Park Ave.
New York.
DISEASES DUE TO INTOXICATION
Robert A. Kehoe, M.D.
The Kettering Laboratory
University of Cincinnati College of Medicine
Eden Avenue
Cincinnati 19.
EAR, NOSE, AND THROAT
M. M. Hipskind, M.D.
55 E. Washington
Chicago.
ENDOCRINE
Arthur Grollman, M.D.
Southwestern Medical School of the University of Texas
Department of Experimental Medicine
2211 Oaklawn Ave.
Dallas 4, Texas.
EYE
John H. Dunnington, M.D.
Institute of Ophthalmology
Presbyterian Hospital
635 W. 165 St.
New York 32.
FEMALE GENITAL
J. P. Greenhill, M.D.
55 E. Washington St.
Chicago.
HEART
Harold E. B. Pardee, M.D.
770 Park Ave.
New York 21.
HEMIC AND LYMPHATIC
Louis R. Limarzi, M.D.
30 N. Michigan Ave.
Chicago.
MUSCULOSKELETAL
H. Earle Conwell, M.D.
Conwell Orthopedic Clinic
2031 11th Ave., South
Birmingham 5, Alabama.
NEUROLOGY
H. Houston Merritt, M.D.
Director of Neurological Service
Columbia-Presbyterian Medical Center
New York 32.
ONCOLOGY
E. Cuyler Hammond, M.D.
Statistical Research Section
Medical and Scientific Department
American Cancer Society, Inc.
521 W. 57th St.
New York 19.
PARASITOLOGY
W. H. Taliaferro, M.D.
Department of Bacteriology and Parasitology
University of Chicago
5724 Ellis Ave.
Chicago 37.
PATHOLOGY
Paul R. Cannon, M.D.
Department of Pathology
University of Chicago
Chicago 37.
PSYCHOBIOLOGIC UNIT—PSYCHIATRY
George N. Raines, M.D.
Bureau of Medicine and Surgery
23rd and E Streets, N.W.
Washington 25, D. C.
RADIATION
Gilbert H. Fletcher, M.D.
University of Texas
M. D. Anderson Hospital
Houston 25, Texas.
RESPIRATORY
John D. Steele, M.D.
V. A. Hospital
San Fernando, Calif.
SKIN
Herbert Rattner, M.D.
104 S. Michigan Ave.
Chicago 3.
TOXICOLOGY
Irvin Kerlan, M.D.
Food and Drug Administration
Washington 25, D. C.
UROLOGY
Montague L. Boyd, M.D.
2560 Habersham Road, N.W.
Atlanta 5, Ga.

QUARTERLY CUMULATIVE INDEX MEDICUS

Volume 60 of the Quarterly Cumulative Index Medicus, covering literature for the second half of 1956, has been mailed to subscribers and is now available for purchase from the Circulation-Records Department of the American Medical Association.

BUREAU OF INVESTIGATION

BE A SPECIALIST—THE EASY WAY

AND AT SUCH A BARGAIN, TOO—ONLY $250!

A firm in Albuquerque, N. Mex., called Rittenhouse & Revere, Inc., has been distributing a form letter printed in red and black, offering to make specialists out of interested physicians. This blurb offers means whereby "any M.D. PHYSICIAN—Anywhere Can Quickly Build a Large and Remunerative Specialty Practice Such as Obesity, Rectal, Arthritis, Headache, etc. . . ." and bears the facsimile of the signature of Mr. Charles F. Johnson, president.

The program is, according to the announcement, a means whereby the "M.D. Physician" will get new patients—in fact, it will go so far as to select patients with afflictions preferred by the physician and give the recipient physician a little preview of his patient before he sees him. Physicians are also reminded that they are probably working too hard and can lighten their labors and at the same time increase the size of their bank balances and be spared the necessity of advertising—and thus avoid becoming unethical!

If the interested "M.D. Physician" will send a check for $250, Mr. Johnson will visit his office and give him details of the plan. If, for instance, he chooses obesity as a specialty, he will receive some medicines for treating this category, "without additional charge."

The Bureau of Investigation has had data in its files for several years which reveal the method, so far as "drugless healers" are concerned. The November-December, 1947, issue of the *Pasadena World* carried an item on the firm, as follows:

> "SINUS SUFFERERS. In the Pasadena area. If you want Relief or Help—Send for Free Sinus Book. We have no medicine or anything else to sell you."
>
> Thus read an ad in a Pasadena paper of Rittenhouse & Revere of Albuquerque, N. M.
>
> When you receive the pamphlet you read some alarming facts, enough to scare you into seeing a doctor pronto.
>
> And enclosed with the booklet is a "Dear Friend" printed letter recommending you go to Dr. Chas. J. Clark, the chiropractor, at 189 N. Los Robles. It says we are indeed fortunate in having him in Pasadena.
>
> It seems for sinus trouble he uses "Nascent Haloid Vapor Germicidal Respiratory Therapy"—the machine for which is sold by Rittenhouse & Revere.

The file does not reveal the amount of enthusiasm generated in Pasadena over chiropractor Clark, but it does show a willingness on the part of Rittenhouse & Revere to do their share as business builders.

In 1948 an osteopath wrote in in wonderment because he had received an offer to increase his practice, as follows: "Sixty days from today, you can have a $30,000 a year practice organized, started, and well under way, or, stating it another way—you can be adding $30,000 yearly to your present income." This five-page offer from Mr. Johnson, president of Rittenhouse & Revere, included an order blank for an electrochemical apparatus, including an instruction manual. The combination cost was either $350 for a duplex model or $250 for a single model. This machine was supposed to perform therapeutically in the treatment of sinus and upper respiratory infections, arthritis, rheumatism, and kindred afflictions and to relieve pain, as well as asthma, hay fever, bronchial congestion, and perhaps a few other conditions. It was described as a "generator for the electrolysis of various salt solutions and electrochemical dissociations, analysis and depositions."

The therapeutic claims met with some skepticism on the part of the federal Food and Drug Administration. At least, that agency reported in a Notice of Judgment that it had filed a libel action against two such devices found in the possession of a chiropractor in Oklahoma City and shipped by Rittenhouse & Revere in 1948. Earlier it had filed a similar action against a single device, in the southern district of California.

In another such seizure action reported by the federal agency, a libel was filed in the federal district court for the northern district of California. This involved a device that was "designed for vaporizing liquids and for producing galvanic, surge galvanic, sine wave, and faradic voltages." This device was misbranded, according to the federal report, because statements in labeling "represented and suggested that use of the device constituted an adequate and effective treatment for adhesions, amenorrhea, anemia, aphonia, emphysema, bronchiectasis, bronchitis, cataracts, cerebral congestion. . . ." (These claims go alphabetically through intestinal stasis, chronic nephritis, mastitis, prostatitis, to uterine subinvolution and visceroptosis.)

In 1954 Rittenhouse & Revere appeared as claimant and filed an answer denying that the device was misbranded. Later the firm withdrew the answer; judgment of condemnation was entered, and the court ordered that the product be delivered to the FDA.

In 1957 the Los Angeles Better Business Bureau published a note in its weekly bulletin *Data* (vol. 9, no. 38). Attention was called to the fact that Los Angeles area sufferers from arthritis, rheumatism, heart trouble, and other ailments were being attracted by advertising placed by the firm, which suggested that sufferers forward 9 cents in postage, in return for which a health book would be sent which would enable them to understand all the facts about their own case and would also give instructions as to sources of help and relief near home. The Better Business Bureau was informed by persons who answered the offer that in the same mail with the booklet they received a letter from the concern "recommending and extolling the services and 'equipment' of a non-medical doctor in a nearby neighborhood or community."

The Los Angeles bureau went on to describe Mr. Charles F. Johnson, the president of Rittenhouse & Revere, as a former mining engineer, and stated that "the operation is the sale of so-called scientific and therapeutic equipment to non-medical doctors on a 'practice-building plan.' This plan is supposed to increase the non-medical doctor's income by some $30,000 a year." The bureau further commented: "It should not be difficult to deduce that the 'doctors' so highly recommended are those who have purchased the equipment."

One of these letters happens to be in the files of the Bureau of Investigation. This one reads in part:

> Dr. Pierchala, D.C., N.D., M.T., has a reputation of being very successful with his cases and has patients coming to him from many distant places both in and outside of the state. He has modern offices splendidly equipped, and a large practice.
>
> We feel confident that you will find it well worth while to call at his office for a consultation. If you should not be entirely pleased with Dr. Pierchala, let us know. We shall be glad to send you the names of other Doctors, even though none of the others happen [*sic*] to be located within a convenient distance from where you live. We are sure you will like him. Everybody does.
>
> Dr. Pierchala is always busy and we suggest you telephone or write his office today for an appointment.

This letter was sent in answer to an advertisement addressed to "High Blood Pressure (Hypertension) Sufferers." The advertisement added: "We have NO MEDICINE or ANYTHING ELSE to Sell You."

In the current letter inviting "M.D. Physicians" to add to their incomes and become "specialists," there is a footnote on page 3 which reads: "Rittenhouse & Revere, Inc., has a long established Pharmaceutical Subsiduary [sic] Calvin Scott & Co. with one of the largest complete lines of Dispensing Medications in the United States, including a wide selection of the most used OBESITY formulas. All items are sold direct to our physician customers at low wholesale prices."

The Albuquerque telephone directory for October, 1956, lists Calvin Scott & Co., Inc., in the Metropolitan Building, with the telephone number 3-5309. Rittenhouse & Revere also is located in the Metropolitan Building and has the same telephone number.

It seems strange that Mr. Johnson finds it necessary to seek new pastures for the dispensing of his goods, wares, and merchandise. There is no question that his is an approach attractive to naturopaths, chiropractors, and other "fringe" practitioners. The likelihood is that he will find a few doctors of medicine who are so inept in their own methods of practice that a booster in the form of a tailor-made specialty is a necessity. No doubt those whose practice needs such a stimulus will not mind having the type of "referrals" offered by this energetic and enterprising business firm. If this is such a successful method, Mr. Johnson should be more than busy boosting business for the "drugless healers."

COUNCIL ON MEDICAL SERVICE

The Foundation for Medical Care of the San Joaquin County Medical Society, California, has created widespread attention as a result of the prepayment programs it has developed for the public, management, and unions. Over 300 physicians in San Joaquin and Stanislaus counties are participating in the foundation's program. The successful operation of this program has stimulated interest in similar foundations in other California counties. The Los Angeles County Medical Association is the most recent medical society to approve the formation of such a foundation, and at least 13 other county medical societies in California are studying the program at present.

The foundation's program utilizes the California Relative Value Study. At the 1958 Clinical Session, the House of Delegates recommended the conduct of relative value studies by constituent medical associations and instructed the Committee on Medical Practices (a committee of the House) to assist medical societies in carrying out such studies. The first of a series of regional meetings on this subject will be held by the Committee in San Francisco in the early part of April.

The following paper, presented at the Western Pension Conference, is being published in view of its interest to physicians and medical societies throughout the country.

FOUNDATION FOR MEDICAL CARE

Donald C. Harrington, M.D., Stockton, Calif.

On March 1, 1954, the doctors of the San Joaquin County Medical Society set up a separate corporation called the Foundation for Medical Care of San Joaquin County. By broad definition, our foundation could be defined as an organization established by a local medical society for the purpose of assuring the availability of medical care to all people within the jurisdiction of our San Joaquin County Medical Society. At this time, 97% of the active doctors of the medical society are members of the foundation. This corporation was designed specifically to study the problems of bringing medical care within the reach of the population of this area, regardless of their ability to pay. Because of the tremendous growth of voluntary prepayment programs in the field of health, one of the first studies the foundation undertook was that of current prepayment programs. Specifically, the foundation set about to evaluate present prepayment programs so as to be, eventually, in a position to advise and assist insurance companies and consumers in the selection of a broad base coverage which is so desirable in prepayment programs. The three goals established for the foundation are (1) the formulation of a basis for group prepayment which the foundation would not only recognize but would sponsor and endorse, (2) the formulation of an individual and family prepayment program which the foundation would sponsor and endorse, and (3) the study of methods to bring assistance to many who, for various reasons, are not in a position to have group or individual prepayment programs.

To establish such a program, it was first necessary to find what was the actual fee being charged for medical service in this area. A survey of charges was made—resulting in a fee schedule which was used for two years before being abandoned in favor of the California Medical Association Relative Value Schedule with coefficients appropriate

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President, Foundation for Medical Care of San Joaquin County.
Read before the Western Pension Conference, San Francisco, Dec. 2, 1958.

for the schedule. As soon as the original schedule was adopted, all members of the foundation agreed to charge no more than the fee listed for prepayment programs sponsored by the foundation. Not only does this benefit the patient who has a foundation-sponsored prepayment program, but the other patients, whether covered by insurance or not, are able to ascertain what the usual fees in the area are. Each year the schedule is reviewed and revised where necessary.

The foundation believes that establishing this fee schedule gives voluntary prepaid medical insurance plans a realistic criterion on which to base their policies. It should help improve the type of coverage offered in these policies and, in general, raise the standard of prepaid medical insurance contracts. A person seeking this type of insurance has, under the foundation's plan, the certainty of coverage which he so desperately seeks. He is also able to evaluate any insurance program in relation to what is actually being charged in the area.

While constant work is required on the income levels within San Joaquin County, it is the primary philosophy of the foundation that a prepayment program must have some application to the incomes of the various families. These various income levels must be applied to reasonable premiums for each income level. If the percentage of a family's income, customarily paid on medical care, reaches a figure that is wholly out of the question from an insurance standpoint, then some other practical solution must be taken. In carrying out this belief, the foundation adopted three schedules—schedule 3 for persons making a gross family income of $4,500 or more, schedule 2 for those with an income of $3,500 to $4,500, and schedule 1 for those with an income under $3,500.

One of our most important concepts is based on the belief that most physicians are willing to adjust fees downward for people with low incomes. The foundation believes that a great deal of medicine's predicament is due to the inability of doctor and patient to "get together" on their financial arrangements; i. e., both are reticent about discussing it. Because of this reticence, an administrative mechanism that sets up guideposts is needed. The foundation has, therefore, established a fee schedule which represents an accumulation of fair fees for this area. By and large, these fees represent what is actually being charged. Above this schedule, the doctors cannot go. Any adjusting of the schedule is downward for reasons already stated.

The problems of adjusting fee schedules to income are many and obvious. However, there is no other index that can be used effectively, so the foundation has used it as a rough "means test." To put this into practice, being fair to both patient and profession, is difficult as there are many unknown and large areas where no information is available.

The foundation used the information in the Heller Report, 1948, and the more recent survey by the Health Information Foundation. This sets a figure of 4%, excluding cost of drugs, dental work, and glasses. This is probably low, as it, for the most part, includes mostly uninsured groups at the present incidence of usage. This will, obviously, increase with usage up to a desired point for good health.

A "co-insurance base" was determined with use of the 4% figure. With use of this base (it finally worked out to 3.8%, including insurance administrative costs), tentative fee schedules and premiums were developed and the number of people involved in each income group was predicted.

In attempting to apply the practice of medicine to income levels, it is necessary to recognize that certain procedures are procedures of high overhead and others are of low overhead. For instance, in a San Joaquin County survey of procedure costs, a routine office visit costs approximately $2.57.

The foundation has felt from the beginning that a sound program could not be established by merely adopting a fee schedule or schedules and attaching the "prior agreement" principle. The mechanism of "prior agreement with an insured group" was the result. If an insurance company is willing to write a policy based upon the foundation's three schedules, including the co-insurance and deductible features which the foundation feels are necessary, this prior agreement with a group then becomes an endorsement of the policy. The physicians of the foundation would charge no more than was stipulated in the contract.

Thus, an indemnity program becomes a service program. The deductible and co-insurance features are clearly delineated so that the patient then knows exactly how much the fee will be. On items not covered by insurance, such as house and office calls for the dependent, the fee percentages still apply so that a dependent of an employee, insured under schedule 2, will be charged no more than schedule 2 rates for an office or home call.

Basic Group Programs

On Sept. 1, 1954, the Continental Casualty Company wrote the first program for the foundation. It covered the Lathers, Plasterers, and Hodcarriers' Union of San Joaquin County at a premium of $11.34. This program fell in schedule 2. Four years later this particular program is still underwritten at the same premium. During that time the fee schedule has been raised and an additional $1.20 worth of benefits has been added within the original premium structure. Since the income of this group is rising steadily, it is anticipated that they will soon be transferred into a schedule 3 program. In October, 1954, a second program was sponsored —on a schedule 3. Since the group was small and included a high percentage of women, the premium was $15.26. This premium has also remained constant.

A third program was put into effect July 1, 1955, involving Turner Hardware Company, with stores located in Calaveras, Tuolumne, Stanislaus, and San Joaquin counties. The income of the executives pulled this group up into schedule 3, making the premium higher than the group could realistically budget. Because of this, the executives elected to be covered under a schedule 3 program while the store's many employees were covered under a schedule 2 program. This had created no administrative difficulty. Since this program is also in effect in Stanislaus County, the medical society of that county has accepted the foundation program and 90 of 144 physicians in that county are now members of the foundation.

There are now eight companies offering the foundation program; they are the Occidental Life Insurance Company of California, Continental Casualty Company, Pacific National Life Assurance Company, Pacific Mutual Life Insurance Company, Intercoast Life Insurance Company, California Physicians' Service, California Western States Life Insurance Company, and Connecticut General Life Insurance Company. Several other companies have expressed interest in underwriting the program.

What does this program mean to the doctors? It gives them local control and it supplies them with a fee list that is based on what is actually charged in their area. The program can be underwritten by any insurance company; it is flexible and can react quickly to local situations. When underwritten by an insurance company, it is an indemnity program which can be used outside the foundation membership and outside of this area.

Comprehensive Major Medical-Group Program

There appears to be public demand for what the insurance industry has termed comprehensive major medical coverage. At the same time various insurance companies have taken the position that quality control is necessary for the survival of this type of coverage. For these reasons the foundation sponsored its first major medical program in January, 1958. Minimum requirements for foundation sponsorship include a fee schedule based on schedule 3, co-insurance by the patient not to exceed 20%, no more than a $50 deductible clause per person per year, and maximum benefits of at least $5,000. It is the current opinion of the foundation that this type of coverage should not be offered to the low income groups.

Basic Plus Major Medical Coverage

Several groups have availed themselves of this type coverage, and experience thus far with the programs seems to be satisfactory. Probably our most interesting program at the moment is one covering the warehousemen in our area. The International Longshoremen's and Warehousemen's Union–Pacific Maritime Association (ILWU-PMA) Welfare Fund has worked out a program with the foundation giving basic coverage to this group with a superimposed major medical. In our minds this is a much sounder approach for the lower income groups that a comprehensive major medical program with a $50 deductible.

Quality Controls

According to the bylaws of the foundation, membership is on a one-year basis. This is specifically designed for internal control as each physician must reapply every year. This approach towards quality control within the profession, by the profession, is also furthered by a program of claims review. These are only two of the steps in the direction of self-discipline which the physicians of the foundation feel are of paramount importance if the profession is to continue its emphasis on the private practice of medicine. The membership on a one-year basis also gives the participating doctor an opportunity to reaffirm his faith in the foundation.

Initially, the foundation reviewed only questionable billings. This proved to be ineffective. The foundation soon realized that many physicians were making mistakes in their billing that were due mainly to lack of understanding of the program and of prepayment in general. These mistakes were being taken by those outside of medicine as examples of malicious intent. The foundation now processes all claims. Each claim is reviewed from both a contractual and medical standpoint, the latter by a physician of the foundation. In order to facilitate this part of the program, draft authority has been procured from each of the participating underwriters. This means that the foundation office not only processes the claims but pays the doctor on an assignment of benefits. The foundation has written into its agreement that if a patient refuses to assign his benefits, the doctor is not bound by his agreement with the foundation to accept the fee as full payment.

An Individual Program

In pursuit of the second goal of the foundation, that of bringing forth a good individual policy to be offered in this area, the foundation was pleased to announce that, as of Sept. 1, 1955, the California Physicians' Service would offer a rather unique individual policy in San Joaquin County. This policy is based on the same approach of income level as was used in the group insurance.

A rather extensive selling campaign was carried on by both the California Physicians' Service and the Foundation for Medical Care. The policy was sold through selected brokers. The policy was offered to each individual and his family with the same varying income levels; hence, the premiums for the various policies vary. For instance, under schedule 3 a single male pays $5.95 per month; under schedule 1 a single male pays $4.85 per month. For three or more in the family, the cost is $14.50 under schedule 3 and $11.15 under schedule 1.

The individual program pays surgical benefits in full and has rather comprehensive in-hospital benefits. The unique feature of the program is that there was now available to individuals an adequate outpatient diagnostic and x-ray laboratory benefit. There was also an allowance for 50 physi-

MEDICINE AND THE LAW

SURVEY OF PROFESSIONAL LIABILITY INSURANCE

Approximately 40 companies write medical professional liability insurance in the United States. To evaluate the strictness or liberality with which insurers interpret the basic policy provisions relating to coverage and exclusions, the Law Division of the American Medical Association sent a questionnaire to 35 insurers. Some responded that they had discontinued writing such insurance or that the number of policies they had in force was so small that they did not believe themselves qualified to speak on the subject; several politely but firmly declined to complete the questionnaire. However, 22 companies responded to the questionnaire and in terms of number of policies they probably account for more than 80% of the policies in force.

The responses indicate that the malpractice insurance protection which the physician purchases is determined not only by the policy provisions but to a large extent by the underwriting philosophy of the company. In commenting on the questionnaire, one respondent stated:

> Consider, if you will, the consternation that would result if you prepared 14 different sets of symptoms representing 14 fine-line medical cases and asked a representative group of doctors what they would do in each instance. I am sure that any replies which you received would be full of "if's," "and's" and "but's." Policy drafting is no more an exact science than medicine. I don't know how many insurance companies received your questionnaire but if a large number reply, including perhaps some that have only recently undertaken to write physicians' and surgeons' liability, I don't envy you your job in trying to reconcile the answers. You might get a different answer from the same company depending on whether the reply was made by a claims attorney or an underwriter. As to my company, if it is the underwriting intent to give coverage in a particular instance, then that intent prevails even though a strict construction of the policy wording might offer an "out."

While the above respondent is primarily concerned with underwriting intent, the respondent whose comments follow considers its policy obligations in a more literal sense.

> Whether a claim is covered for the purpose of defense is determined by the allegations of the injured party's complaint. If these allegations are of something which would be covered by the policy, the Company owes a defense, however false and fraudulent the allegations are. If, however, the complaint alleges something not covered by the policy and does not allege anything else, no defense is owed. This is founded in reason and is the universal decision of the courts of this country, with the exception of one or two poorly reasoned cases. There is no difference between the defense provision in malpractice policies and the defense provision in other general liability policies.
>
> To illustrate the matter a little further, if the injured party alleges nothing covered by the policy, there is no defense; if the injured party alleges two grounds of action, for example in different counts of the declaration, one of which would be covered by the policy if true and the other of which would not, the Company is bound to enter a defense. In such event the Company would defend under a reservation of rights. This is because it may turn out at the trial that the injured party had an actual claim only on the ground which was not covered by the policy, so that the insurer will not have to pay the judgment.
>
> In answering the questions we have assumed that the injured party is not alleging any other ground than that stated in the question. We therefore have answered the question simply on whether or not there is coverage on the allegations of the plaintiff stated in the particular question, except in one or two cases, since, if there is not coverage, there is no obligation to defend.

Although based on actual claims and cases which have come to the attention of the A. M. A. Law Division, the questions are hypothetical. With reference to each of the numbered fact situations set forth below, the company was asked for its opinion regarding coverage, or the insurer's obligations to defend and pay the judgment, if any, within policy limits. The responses are summarized and some of the significant remarks made by the respondents are included, as well as the comments of this writer.

Questions

1. Dr. Benson, a general practitioner, was called to treat Peter Smith. When he arrived he found what appeared to be an acute psychiatric emergency. Subsequently, Peter Smith brought an action against Dr. Benson charging personal restraint and false imprisonment.

Six companies said "yes," without qualification, regarding coverage. Sixteen companies qualified their answers in varying degrees, as indicated by the following excerpts from their replies:

> Coverage is given as long as the action of the doctor is within the normal activities of a doctor.
>
> Yes. Except where insured has stepped outside the bounds of his profession, as he would if his action is prompted by personal bias, and except where the insured's action amounts to performance of a criminal act, such as conspiracy. In actual practice, we have defended the vast majority of cases of this type to a conclusion, since the exceptions eliminating coverage are rarely, in fact, established.
>
> Yes. We would defend under a Reservation of Rights if a criminal act is alleged but our insured, the doctor, denies the criminal act.
>
> If the insured's report, our investigation or the allegations of the complaint disclosed a criminal act no insurance therefor would be provided by the policy.
>
> Frequently, when claims are presented, among the allegations will be found one involving a criminal act. Rarely if ever is a criminal act the sole basis of a claim. Even then said criminal act is simply an allegation and not a fact until the point has been adjudicated. In such cases it would be

cian visits on an outpatient basis for certain catastrophic diseases. This individual program, however, still limits initial enrollment to those under age 60, requires a health statement, and by and large is, as all other individual insurance, much more costly than group coverage. This program has gained momentum slowly.

The International Longshoremen's and Warehousemen's Union–Pacific Maritime Association Program

A new program unrelated to the original foundation approach went into effect July 1, 1955. At that time the Foundation for Medical Care signed a one-year contract with the International Longshoremen's and Warehousemen's Union–Pacific Maritime Association (ILWU-PMA) Welfare Fund to provide medical and surgical care to the longshoremen of the Stockton area. This program was a pilot program for one year only, but it has been so successful that it is still in force and with many added benefits. At the present time the program pays on the basis of *schedule 3.* Stockton is the third largest port in California at this time, employing between 600 and 700 longshoremen, ships clerks, and walking bosses. Up to now these men and their families have had an insured health plan with a set schedule of benefits payable toward their expenses for hospital, medical and surgical care.

In 1955, the Trustees of the ILWU-PMA Welfare Fund approached the foundation with a proposal for a comprehensive type of medical and surgical service plan. The fund's proposal was based on a desire for certainty of coverage which was not furnished by their insurance. The fund wanted to prepay all or a great part of the costs of medical and surgical care and to assure the families that any out-of-pocket expenses for this care would be limited and predictable. Another consideration in the proposal was provision of services which are not insurable, such as well baby care. The agreement drawn up between the foundation and the fund, after long study, embodies this proposal and meets the foundation's standards of sound practice of medicine on a sound financial base. The agreement went into effect July 1, 1955, for one year.

Any member of the medical society may become a member of the foundation and then may care for any longshoreman and his dependents (wife and unmarried children up to age 19) under the new program. All of the eligible members of the union, including those on retirement, are covered. Men and dependents can go to any physician who has elected to become a foundation member, and the coverage applies to services given by those physicians. The foundation's service area is San Joaquin County, however, provision for referral to physicians outside the service area and coverage for their services is provided as required.

Under this contract, as in all endorsed and individual contracts of the foundation, patients are automatically excluded from county hospital services, except for contagious diseases and emergencies. Hospital benefits are not part of the foundation-fund agreement. Hospital room and board and services remain insured, as do a $2,000 poliomyelitis benefit for dependents, and "catastrophic coverage" for men in hospital cases. Patients can use any licensed hospital.

The fund has allotted for the Stockton program $13.00 per month per man, to include family coverage. Of this amount, $5.69 goes to Pacific National Life Assurance Company for the insured items (hospital, "catastrophic," etc.) and $7.31 will go to the foundation for provision of medical and surgical services. The foundation will pay its participating members furnishing services under the agreement on a fee-for-service basis. All claims for services rendered are reviewed each week by a three-doctor committee of the foundation.

The agreement covers off-the-job conditions. It does not cover job-connected disabilities, dental care, routine checkups (except for well babies), refractions, or services for drug addiction, alcoholism, mental conditions, sterility, contagious diseases requiring isolation for hospitalized patients, or conditions resulting from major disasters or epidemics. Detailed records on costs and utilization under the agreement are being kept by the foundation.

Summary

The foundation has, since its organization on March 1, 1954, (1) *set up a fee schedule* based on the California Medical Association Relative Value Study, using coefficients which reflect the private practice fees of this area, (2) *stimulated* acceptable group insurance programs, based on this schedule, which are being offered by six insurance companies and the California Physicians' Service, (3) stimulated a family and individual contract offered by California Physicians' Service, (4) embarked on a service contract for medical care with International Longshoremen's and Warehousemen's Union–Pacific Maritime Association Fund, and (5) set up an advisory committee made up of interested citizens in the community, namely, a clergyman, an industrialist, a labor leader, a personal representative from city government, a public relations executive, a department store executive, a representative of the teaching profession, and a pharmacist. Projected for the future is the inclusion of the noninsured into the program by social service methods, the utilization of insurance methods in the care of the indigent, and the coverage of the retired and aged by prepayment.

Medicine is a harsh taskmaster, taking its toll on our time and our health. Adequate compensation to the doctor is essential. But, I feel, it is a privilege to practice medicine. With this privilege comes a responsibility of caring for people within the range of their ability to pay. In the face of ever-increasing coverage of prepaid medical care insurance, it behooves organized medicine to actively work with the insurance company, the Blue Shield Plans, and the consumer.

936 N. Commerce St.

MEDICINE AND THE LAW

SURVEY OF PROFESSIONAL LIABILITY INSURANCE

Approximately 40 companies write medical professional liability insurance in the United States. To evaluate the strictness or liberality with which insurers interpret the basic policy provisions relating to coverage and exclusions, the Law Division of the American Medical Association sent a questionnaire to 35 insurers. Some responded that they had discontinued writing such insurance or that the number of policies they had in force was so small that they did not believe themselves qualified to speak on the subject; several politely but firmly declined to complete the questionnaire. However, 22 companies responded to the questionnaire and in terms of number of policies they probably account for more than 80% of the policies in force.

The responses indicate that the malpractice insurance protection which the physician purchases is determined not only by the policy provisions but to a large extent by the underwriting philosophy of the company. In commenting on the questionnaire, one respondent stated:

> Consider, if you will, the consternation that would result if you prepared 14 different sets of symptoms representing 14 fine-line medical cases and asked a representative group of doctors what they would do in each instance. I am sure that any replies which you received would be full of "if's," "and's" and "but's." Policy drafting is no more an exact science than medicine. I don't know how many insurance companies received your questionnaire but if a large number reply, including perhaps some that have only recently undertaken to write physicians' and surgeons' liability, I don't envy you your job in trying to reconcile the answers. You might get a different answer from the same company depending on whether the reply was made by a claims attorney or an underwriter. As to my company, if it is the underwriting intent to give coverage in a particular instance, then that intent prevails even though a strict construction of the policy wording might offer an "out."

While the above respondent is primarily concerned with underwriting intent, the respondent whose comments follow considers its policy obligations in a more literal sense.

> Whether a claim is covered for the purpose of defense is determined by the allegations of the injured party's complaint. If these allegations are of something which would be covered by the policy, the Company owes a defense, however false and fraudulent the allegations are. If, however, the complaint alleges something not covered by the policy and does not allege anything else, no defense is owed. This is founded in reason and is the universal decision of the courts of this country, with the exception of one or two poorly reasoned cases. There is no difference between the defense provision in malpractice policies and the defense provision in other general liability policies.
>
> To illustrate the matter a little further, if the injured party alleges nothing covered by the policy, there is no defense; if the injured party alleges two grounds of action, for example in different counts of the declaration, one of which would be covered by the policy if true and the other of which would not, the Company is bound to enter a defense. In such event the Company would defend under a reservation of rights. This is because it may turn out at the trial that the injured party had an actual claim only on the ground which was not covered by the policy, so that the insurer will not have to pay the judgment.
>
> In answering the questions we have assumed that the injured party is not alleging any other ground than that stated in the question. We therefore have answered the question simply on whether or not there is coverage on the allegations of the plaintiff stated in the particular question, except in one or two cases, since, if there is not coverage, there is no obligation to defend.

Although based on actual claims and cases which have come to the attention of the A. M. A. Law Division, the questions are hypothetical. With reference to each of the numbered fact situations set forth below, the company was asked for its opinion regarding coverage, or the insurer's obligations to defend and pay the judgment, if any, within policy limits. The responses are summarized and some of the significant remarks made by the respondents are included, as well as the comments of this writer.

Questions

1. Dr. Benson, a general practitioner, was called to treat Peter Smith. When he arrived he found what appeared to be an acute psychiatric emergency. Subsequently, Peter Smith brought an action against Dr. Benson charging personal restraint and false imprisonment.

Six companies said "yes," without qualification, regarding coverage. Sixteen companies qualified their answers in varying degrees, as indicated by the following excerpts from their replies:

> Coverage is given as long as the action of the doctor is within the normal activities of a doctor.
>
> Yes. Except where insured has stepped outside the bounds of his profession, as he would if his action is prompted by personal bias, and except where the insured's action amounts to performance of a criminal act, such as conspiracy. In actual practice, we have defended the vast majority of cases of this type to a conclusion, since the exceptions eliminating coverage are rarely, in fact, established.
>
> Yes. We would defend under a Reservation of Rights if a criminal act is alleged but our insured, the doctor, denies the criminal act.
>
> If the insured's report, our investigation or the allegations of the complaint disclosed a criminal act no insurance therefor would be provided by the policy.
>
> Frequently, when claims are presented, among the allegations will be found one involving a criminal act. Rarely if ever is a criminal act the sole basis of a claim. Even then said criminal act is simply an allegation and not a fact until the point has been adjudicated. In such cases it would be

> our policy to defend our insured but to reserve our rights under the policy should our insured be found guilty by a duly authorized court of having performed a criminal act.
>
> We would normally expect to defend an insured accused of a criminal act, if he denies it. Until the contrary is proven or admitted we would not expect to pay a judgment which was founded upon the performance of a criminal act by the insured.
>
> The case supposed in the question, if it is unlawful detention, appears to be so only in a civil sense, and it also happens to be malpractice in our viewpoint. However, there can be any number of cases of false arrest or unlawful detention connected with a physician's practice, which would not constitute malpractice within a proper construction of the insuring agreement, or which would be excluded as a criminal act. For example, a physician might have a patient arrested for allegedly giving him a bad check in payment of his bill. This could not possibly be construed as malpractice.
>
> The determining factor would be whether in fact a criminal act is involved. In drafting this particular policy form, the criminal act exclusion was included as a protective measure to exclude those acts which clearly go beyond the border of good professional conduct. It was not the intention that the exclusion would be literally and technically applied but that it would be used in those cases where it seemed necessary and proper to do so.

Comment.—It is not unusual for a physician to be called to help cope with the situation when some member of the family has apparently and suddenly gone berserk. Legal actions have evolved out of these cases, in which the physician has been charged with the use of excessive force or false imprisonment.

It is clear that Dr. Benson came on the scene to render professional services of a nature frequently performed by physicians. However, the professional liability policy specifically excludes coverage of "criminal acts," even though they may arise out of the practice of medicine. If Dr. Benson did in fact apply excessive force and restraint, technically this would amount to a "criminal act" in most jurisdictions, even though the possibility of prosecution or conviction might be remote.

2. Dr. Collins operated on Mrs. King, with her consent, for an ovarian cyst. In the course of the operation he found that a radical hysterectomy was advisable and thereupon performed this procedure. Mrs. King brought suit against Dr. Collins charging assault and battery in that he went beyond the consent given.

Twelve companies responded that they would defend the physician and pay the judgment. The other insurers generally did not refuse coverage but qualified their position with such statements as these:

> The answer to this question would depend upon whether the performance of the radical hysterectomy without the consent of Mrs. King was a criminal act in that jurisdiction. Assuming that it only gave rise to a civil suit for damages, we would think that it was malpractice not excluded by the policy.
>
> In such cases it would be our policy to defend our insured but to reserve our rights under the policy should our insured be found guilty by a duly authorized court of having performed a criminal act.
>
> If the insured's report, our investigation or the allegations of the complaint disclosed a criminal act no insurance therefor would be provided by the policy.

Comment.—Despite the good faith of the surgeon who may be acting in the interest of the patient if, in the absence of an emergency, he performs an operation substantially different from the one to which the patient consented, he may be guilty of a technical assault and battery. Situations of this kind have arisen in the course of operations under circumstances where the patient is anesthetized and the surgeon assumes that the patient would prefer to have him proceed than undergo another operation. If the operative result is poor the patient's attorney may prefer to allege unauthorized surgery than to attempt to prove negligence.

In one case[1] a patient consented to the defendant's operating on her foot for the purpose of draining an infected wound but instructed the defendant not to remove any bones. The defendant removed the sesamoid bone because the drainage could not be accomplished unless he did so. This was held to be actionable, even though there was expert testimony that the sesamoid bone serves no useful purpose. In another[2] it was held that the patient's consent to an operation on her right ear did not authorize the performance of a similar operation on her left ear.

3. Dr. Allen examined Mrs. Jones for a possible female disorder. Later she brought suit for damages against Dr. Allen, claiming undue familiarity.

Seven companies responded that they would defend and pay the judgment, if any. Eleven companies indicated that they would defend if they were convinced that the allegations were untrue, but that they would not pay any judgment that might result. The other four insurers interpreted their policy obligations as follows:

> If our investigation indicated that the doctor was actually not guilty of undue familiarity, we would defend unless the doctor was convicted in a criminal prosecution; however, under such circumstances, we would not pay the judgment.
>
> If the doctor denied the patient's allegations we would defend the suit. Whether or not we would respond in payment of an adverse verdict would largely depend upon the facts developed during the trial of the lawsuit.
>
> Assuming that acts of undue familiarity constitute a crime in the jurisdiction involved, this suit would not be covered.
>
> Such a claim would not be covered if a criminal act such as rape or attempted threat was committed. However, if the "undue familiarity" consisted of certain acts considered normal in performing such an examination, there would be coverage under our policy.

Comment.—Physicians are continually cautioned by their medical societies and insurers to avoid examining female patients unless a third person, such as a nurse, is present. Claims alleging undue familiarity are frequently no more than extortion threats. A physician who is convicted of a rape charge may not be entitled to defense or indemnification if the complaining witness brings a civil suit against him. But to what extent should the physician who is only civilly involved in a suit charging undue familiarity be able to rely on his insurer for defense and indemnity? Apparently this is an area in which there is no specific answer at this time.

4. Dr. Elliott performed an abortion on Mrs. Arthur which resulted in her death. Mr. Arthur brought a death action charging an illegal abortion. In asking the company to defend him, Dr. Elliott claimed that there was a therapeutic need for the abortion.

Twelve respondents stated that they would defend but would not pay any judgment that might be rendered. Seven companies would defend only if they believed that the physician had not committed a criminal act, but indicated that they would not be liable to provide coverage against any judgment that might be rendered. Two companies would neither defend the physician nor pay any judgment, inasmuch as a criminal act was alleged and such actions are not covered by the policy. One company interpreted its liability to cover both defense and payment if a judgment is awarded. Typical of the comments of the respondents were these:

> Any charge against the doctor in a suit for damages must be based on his having done something illegal.
>
> We assume that an illegal abortion would be a crime in any jurisdiction. This being so, there would be no obligation to defend a suit alleging an illegal abortion, and, of course, no obligation to pay a judgment. Dr. Elliott's claim that there was a therapeutic need for the abortion is merely a plea by him that he did not commit the crime. Since nothing but the crime is alleged in the declaration, there is no coverage whether or not Dr. Elliott wins the suit.
>
> As long as the doctor says it was necessary for therapeutic reasons we would defend the case, but if the jury found that the operation was not for therapeutic reasons we would not pay any judgment on the assumption that the operation was illegal.

Comment.—Even though an illegal abortion is clearly a criminal act and is therefore excluded by the policy, only two companies would refuse to defend a physician who denied the charge. Considering the obligations which an insurer has to its other policyholders or stockholders, is it justified in gratuitously assuming the defense of a claim excluded by the policy?

5. Dr. Forgan performed an operation for nontherapeutic sterilization on Mrs. Sutter who wanted to avoid further additions to her family of eight children. An accidental injury occurred in the course of the operation and Mrs. Sutter brought suit for injuries because of alleged malpractice.

Eight respondents interpreted their liability as covering both defense and payment, even though the sterilization operation was for nontherapeutic reasons. The other companies generally stated that they would provide coverage only "if sterilization is not a criminal act." A few of the representative comments of the respondents follow:

> In the states where we operate, so far as we know, such actions by the doctor have not been adjudged criminal.
>
> We would defend and pay whether or not the doctor claimed a therapeutic need for the operation.
>
> This answer is based on the assumption that a "nontherapeutic sterilization operation" is not criminal. If it constitutes a crime, we would defend the doctor unless he had been convicted in a criminal prosecution.
>
> Yes. Unless act was found to constitute crime of mayhem.

Comment.—In some states, at least, nontherapeutic sterilization operations are not infrequent. The legality of the nontherapeutic sterilization operation still is an academic question in medicolegal circles. The replies indicate generally that insurance protection will be given, at least until such time as the courts or legislature specifically declare such procedures to be illegal.

6. Dr. Monroe was of the opinion that another pregnancy would endanger Mrs. Phillips' life and therefore recommended and performed a vasectomy on Mr. Phillips. Later Mr. Phillips brought suit charging both malpractice and that the operation on himself was unnecessary.

Eight companies acknowledged that the policy covered both defense and payment. The remaining respondents generally stated, as in the previous hypothetical case, that there would be coverage "if sterilization is not a criminal act."

Comment.—Even though a vasectomy is a comparatively minor operation compared to one for sterilization of a woman, some physicians and others have taken the position that if pregnancy will endanger the wife, she is the one who should be sterilized. It has been argued, for example, that if the wife should die and the husband remarry, the new spouse would be deprived of the opportunity to have a family. Apparently the insurance industry will regard such operations as legal until such time as the courts or legislature may decide to express a contrary opinion.

The therapeutic justification for the sterilizing operation in one case [3] was that further pregnancies would be dangerous to the health of the plaintiff's wife. The operation was performed on the plaintiff husband because the operation for sterilization is simpler and less dangerous in the male than in the female. This was held to be not contrary to public policy. The operation did not produce sterility in the husband. In another case, however,[4] the court assumed without discussion that nontherapeutic sterilization is a wrongful act.

7. Dr. Dickinson was sued by Mrs. Gordon for alleged injuries resulting from an attempt to artificially inseminate her.

Seven respondents said "yes," without qualification, to policy coverage. The 15 other respondents stated that coverage would depend on such qualifications as "whether artificial insemination is a criminal act or against public policy," or whether "artificial insemination was deemed the rendering of professional service."

Comment.—Despite the opposition of a large segment of the clergy in the United States to artificial insemination it appears that insurers will generally render insurance protection until such time, if ever, as artificial insemination performed by a physician may be declared by the courts or the legislature as an illegal act.

8. Dr. Gaines performed cosmetic surgery on Miss Barton. The operation failed to improve her appearance and she brought suit, claiming that Dr. Gaines had guaranteed that the operation would improve her appearance. Dr. Gaines denied the alleged guarantee.

Eleven respondents would deny coverage when the suit is based on an alleged guarantee, and therefore would neither defend the doctor nor pay any judgment that might be rendered against him. Nine of the companies responding indicated that they would defend the doctor if he denied the guarantee or if their investigation did not support the allegation but that they would not pay a judgment based on an alleged guarantee of result. Two companies would both defend and pay on behalf of a doctor who unsuccessfully denied an alleged guarantee of result. Following are a few of the comments made by the respondents:

> If investigation did not support the allegation, the company would defend under reservation.
>
> The company would defend such a claim but would reserve its rights in connection with the physician's guarantee that he would obtain a good result. Any judgment based solely upon the guarantee would not be satisfied.
>
> Generally this would not be covered and both answers should be "No." However, if malpractice is alleged additionally to the guaranty, we would answer "Yes" as to the malpractice allegations.

Comment.—The fact that the professional liability policy expressly excludes claims based on a guarantee of results presents a serious problem. Only a charlatan would guarantee a result for the purpose of obtaining a medical fee. However, there are numerous instances in which a physician will offer words of encouragement to a despondent patient. Such words of encouragement may sometimes be misinterpreted by the patient, particularly in cases of cosmetic surgery in which the injured patient will compare the results of the operation to his appearance as it was before the injury and not as it was after the injury. There have been an increasing number of suits charging reputable doctors with alleged guarantees of result, but it appears that more than half the insurance companies responding would not defend in an action based exclusively on an alleged guaranteed result.

9. Dr. Lawrence had a difficult day and to induce sleep he took a barbiturate before retiring. In the middle of the night, while somewhat under the influence of the drug, he was called on to render emergency medical service to the victims of an automobile accident under circumstances in which another doctor was not immediately available. He was sued for malpractice arising from the services he rendered.

Four companies considered the case as being excluded from coverage by the policy exclusion relating to services rendered by a physician while under the influence of intoxicants or narcotics. Two respondents would defend but were uncertain as to whether they would pay any judgment that might be rendered. Three respondents said that the degree to which the doctor was under the influence of the barbiturate would determine their decision regarding coverage. Thirteen acknowledged coverage as to both defense and payment. The significant comments of the respondents are as follows:

> This case involves the exclusion which rules out injur caused by a person while under the influence of intoxicant or narcotics. On the face of the exclusion, the case woul not be covered. However, a court might feel that the remnants of the effect of a barbiturate, when considered i connection with the emergency, were not sufficient to brin the case within the real intent of the exclusion.
>
> The facts in your case in Question #9 involve an emergency without other professional help available. Under suc circumstances it is difficult, if not impossible, to conceive our invoking the "narcotics" exclusion.
>
> Answers would be yes if insured not sufficiently und influence of drug as to affect his skill or judgment.
>
> We do not believe barbiturate is a narcotic such as intended in the exclusion.
>
> Question #9 has to do with the exclusion of an inju "caused by a person while under the influence of . . . narcotics." Is a barbiturate a narcotic? We do not think so.
>
> The company would defend and pay. It is the intent the policy exclusions relating to "Narcotics" to deny coverage where flagrant misconduct in the use of narcotics evident.

Comment.—Barbiturates may come within th broad definition of intoxicants and narcotics, eve though laymen generally think of intoxicants i terms of alcoholic beverages and narcotics in term of such drugs as morphine, opium, or heroin. Th policy excludes claims arising out of services rendered under the influence of intoxicants or narcotics. Most, but not all, of the respondents indicate that they would not interpret the exclusion literall but would apply it against a physician who is drug addict and committed malpractice while und the influence of his addiction.

10. Dr. Johnson is a general practitioner and insured as such. One of the declarations in his policy states that the insured does not perform maj surgery. Prior to the issue of the policy Dr. Johnso performed only minor surgery and did not perfor any appendectomies for about three years. Bein unable to obtain a surgeon to perform an emergency appendectomy on one of his patients, D Johnson undertook to perform the operation himself. A bad result occurred and Dr. Johnson wa sued for malpractice.

None of the 22 respondents would deny coverag under the facts stated. Some of the remarks mad by the respondents follow:

> The policy declarations contain a statement that the insured does not perform major surgery. This is included f rate-making purposes only and is not intended as a restriction upon policy coverage. As to question 10, therefore, [w

would both defend such a claim and pay any judgment in connection therewith subject, of course, to the limits of liability set forth in the policy.

There is no exclusion in the policy to void a claim of this kind assuming no fraud or deceit was involved when doctor completed questionnaire for Professional Liability Insurance.

Yes—in view of the fact that the operation was performed on an emergency basis and not as a regular practice.

His statement in the declaration was made in good faith and when made was true.

Comment.—It does not appear that the situation presented in the question raises any issue in regard to which the respondents disagree significantly.

11. Dr. Howard was away for a Christmas vacation, and left his employee Dr. Snyder in charge. While attending a Christmas party, Dr. Snyder, who had four or five drinks, was called to perform an emergency appendectomy. He realized that he was to a minor degree affected by the alcohol he had consumed, but, because there was no other physician immediately available to take care of the emergency, he felt that he had no other alternative but to go ahead with the operation. The operative result was bad and Dr. Howard was sued for the alleged malpractice of his employee.

Six respondents said "yes" and six said "no" to both defense and payment. The remaining companies would be willing to defend the employing physician but expressed either doubt or refusal to pay any judgment. Some of the companies expressed these reasons for their position:

We would defend if there was a question as to whether the doctor was under the influence of liquor. We would not pay if the court determined that he was.

It should be mentioned that the fact that the operation was performed by an employee of the insured instead of by the insured makes no difference. The exclusion is not limited to injury caused by the insured himself while under the influence of intoxicants, but extends also to injury caused by any person while under the influence of intoxicants, for whose acts the insured is responsible.

We would defend a claim of the type described in question 11 under a reservation of rights to determine whether Dr. Howard knew of a tendency of Dr. Snyder toward the indiscriminate use of alcoholic beverages. If such a propensity is substantiated there would be a denial of coverage under the policy.

The fact that there is an emergency and no other qualified physician was available would have great bearing on out attitude. We would not invoke the "intoxication" exclusion. From a practical point of view this exclusion is aimed at the habitual drunk or alcoholic whose habits were not known to the company when the policy was accepted.

Question #11 involves the "intoxication" exclusion and seems to ask if that exclusion applies against an innocent insured whose employee is the culprit. The exclusion is one that must be interpreted with a sense of proportion. The actual wording refers to any person under the influence of intoxicants who is the cause of the injury. This would seem to exclude coverage for the innocent doctor who left his employee to take over while he was away. Such an application might not be unreasonable if the doctor-employer knew of the propensities of his employee, and leaving him in charge of operations was a reckless disregard of the obvious. Without this factor, I think the policy should cover. Certainly the exclusion cannot be interpreted literally.

Comment.—The policy excludes coverage with regard to claims which arise from the performance of services while under the influence of intoxicants. Some of the companies would interpret the exclusion literally while others to varying degrees would yield to the equitable considerations presented in the case.

12. Dr. Innes, while performing an operation, accidentally permitted an instrument to slip, thereby causing a severe injury to his physician assistant.

Seventeen companies said that this type of claim is covered, one company thought that coverage was questionable, one respondent would provide defense only, and three companies would deny coverage.

We doubt if this injury would be held to be caused by malpractice. The reasonable meaning and intent of the insuring agreement is to cover an injury to a patient of the insured.

Yes. The case involves "injury arising out of malpractice, error or mistake in rendering or failing to render professional services in the practice of the insured's profession."

For defense only.

Yes. We assume that the physician assistant is not an employee of Dr. Innes.

Yes—there is no exclusion applicable under these circumstances and it makes no difference that the injured was a fellow doctor.

Our policy is not limited to claims by patients. The insuring clause refers to injuries arising out of malpractice, error or mistake in rendering or failing to render the professional services.

Comment.—It is significant that the specific language of the professional liability policy is not limited to injuries sustained by patients. Yet a few insurers would apparently read such a limitation into the policy.

13. Dr. Lawrence gave Mr. Smith a preemployment physical examination. The doctor reported to the prospective employer that Mr. Smith was afflicted with syphilis and Mr. Smith was rejected for employment. Because of a mistake which occurred in the laboratory Dr. Lawrence's report that Mr. Smith had syphilis was in error. Mr. Smith brought suit against Dr. Lawrence charging, among other things, libel.

All of the respondents acknowledged coverage, with the exception of one company which would defend the doctor but would not pay any judgment that might result. Two of the respondents explained their position as follows:

The malpractice policy is not a policy covering libel or slander. In a very restricted class of cases a libel might also constitute malpractice and therefore, if not criminal libel, be covered by the policy. Such a case would appear to be stated in Question 13. The doctor appears to be rendering professional services when he makes the physical examination and immediately renders a report. However, there can be any number of cases in which slander or libel has some connection with the physician's practice where the libel or slander would not merely be malpractice. For example, in the very case given Dr. Lawrence might publish his finding of the disease in some manner other than the report to the employer for the purpose of which the examination was made. Such publication would be pure libel and not malpractice, and therefore not covered.

Inasmuch as the policy refers to the unqualified word "injury," there would be coverage with respect to personal injury which would include libel. Thus the company would be required to defend and to pay.

Comment.—Although the standard policy refers to coverage for "injury" arising out of the performance of professional services, there does not seem to be any question that injury includes libel as well as physical injury.

14. Members of the medical staff at the Central Hospital determine the admission or expulsion of physicians from the medical staff. Only members of the medical staff are entitled to hospital privileges. Dr. Mason, a member of the medical staff, was asked to investigate the surgery performed by Dr. Nixon. Dr. Mason's report stated that Dr. Nixon was incompetent and had performed unnecessary surgery. On the basis of this report Dr. Nixon was expelled from the medical staff. He then brought suit against Dr. Mason charging libel.

Eight companies would defend and pay if a judgment were rendered. Two would defend but would not pay any judgment. Two merely stated that a difference of opinion existed regarding coverage and did not indicate their own position. Ten respondents stated that there was no obligation either to defend or to pay on the part of the company, and three of these respondents also noted that they knew of no standard policy which would cover the risk involved. Following are some extracts from the comments received:

Our policy would provide protection for Dr. Mason's individual liability.

On the assumption that the doctor's report was not intentionally and maliciously false, we probably would defend and pay the judgment.

If the opinion is based upon professional knowledge there would be coverage under the policy, but if it should be based upon personal prejudice, maliciousness and intent to harm then it would be an unprofessional act and no coverage should be afforded.

No standard type of insurance is available.

We cannot consider the action of Dr. Mason in this case to be malpractice in rendering professional services. It is merely libel committed by him in the course of his administrative duties which does not result in injury to any patient or to any patient medically examined by him.

Does it not appear conclusive that it would be unwise to provide such coverage under a professional liability policy because it would protect a doctor who provoked litigation by an act that is not a professional service rendered in the practice of his profession? There will always be honest differences of opinion on medical procedures. Remember Pasteur's experience?

Comment.—In the typical community hospital, administrative and housekeeping functions are within the domain of the board of trustees and the hospital administrator. The medical staff is usually self-governing and determines standards of medical care within the institution, evaluates the surgical and medical care rendered by members of the medical staff, and controls admission to or expulsion from the medical staff. The medical staff carries on its responsibilities through one or more committees, depending on the size of the hospital. Most physicians who treat hospitalized patients participate in the activities of the medical staff from time to time.

When the tissue or medical audit committee has found that a particular physician has repeatedly engaged in unjustified surgery, for example, the result is likely to be that the medical staff will either limit or suspend his hospital privileges. The importance of the activities of the medical staff and its committees in assuring good medical care of the hospitalized patient is self-evident. Physicians serve the public not only by treating their own patients but also by applying their professional learning, talents, and experience to the medical affairs of the hospitals which they attend.

All will agree, of course, that the physician who knowingly or unknowingly undertakes surgery beyond his experience and capabilities should be curbed. But the physician involved may not agree with the decision of his fellow physicians which limits him professionally and thereby economically.

The instant case is hypothetical, but it is based on a few situations which have recently occurred and which are likely to occur in the future in great number as the needs and complexities of modern medicine and surgery require stricter discipline within the self-government of modern hospitals. From the replies received from the insurance carriers the average physician has no assurance whatsoever as to whether his professional liability insurance will cover him in an activity which most practicing physicians may be called upon to perform from time to time. This is an area in which specific insurance coverage should be available.

Conclusions

It is inevitable that there always will be shades of difference among insurance carriers in the interpretations they place on standard policy provisions. In the case of medical professional liability insurance it appears that some of the provisions relating to coverage and to policy exclusions are susceptible of too wide a difference in interpretation.

The results of the questionnaire sent by the A. M. A. Law Division to the companies writing medical professional liability insurance indicate that there are important areas in which the professional liability policy should be clarified and amplified regarding coverage, indemnity, and defense.

References

1. *Rolater v. Strain,* 137 Pac. 96 (Okla., 1913).
2. *Mohr v. Williams,* 104 N. W. 12 (Minn., 1905). See also *Wall v. Brim,* 138 F. (2d) 478 (5th Cir., 1943) and *Perry v. Hodgson,* 148 S. E. 658 (Ga., 1929).
3. *Christensen v. Thornby,* 255 N. W. 620 (Minn., 1934).
4. *Wiley v. Wiley,* 139 P (2d) 950 (Cal., 1943).

MEDICAL NEWS

CALIFORNIA

Researchers Receive Awards.—Dr. Henry S. Kaplan, head, department of radiology, Stanford Medical School, received the second annual Bertha Goldblatt Teplitz Memorial Award "for meritorious investigation in cancer research." The award, including a $500 honorarium, was made by the Ann Langer Cancer Research Foundation of Chicago. The Rubin Award of the American Society for the Study of Sterility was presented to Dr. Robert W. Noyes and his research associates, Dr. Thomas H. Clewe and Aileen Yamate. Dr. Noyes is an associate professor of obstetrics and gynecology. The latter research group was cited for work described in their published paper, "Ovarian Transplants to the Anterior Chamber of the Eye," which appeared last year in the journal *Fertility and Sterility*. The award carries a $250 honorarium.

ILLINOIS

State Medical Election.—Dr. Joseph T. O'Neill, Ottawa pediatrician, was installed as president of the Illinois State Medical Society, succeeding Dr. Raleigh C. Oldfield, Oak Park. The society chose as president-elect Dr. Henry C. Hesseltine, professor of obstetrics and gynecology, University of Chicago, The School of Medicine, who will assume the presidency in May, 1960. Other officers elected are: Dr. Lee N. Hamm, Lincoln, first vice-president; Dr. Allison L. Burdick, Chicago, second vice-president; Dr. Harold M. Camp, Monmouth, secretary-treasurer. Dr. Camp has been secretary of the society for the last 35 years. Dr. Burtis E. Montgomery, Harrisburg, was reelected chairman of the council.

Society News.—On April 15, 1959, the following officers of the Illinois Psychiatric Society were elected for the year 1959-60: president, Dr. Frances Hannett, Chicago 15; president-elect, Dr. Joel S. Handler, Chicago 11; secretary-treasurer, Dr. Paul E. Nielson, 912 S. Wood St., Chicago 12; and councilor, Dr. Nathaniel S. Apter, Chicago 2.——At its annual meeting in Milwaukee, April 17, the Chicago Society of Physical Medicine and Rehabilitation elected the following officers: president-elect, Dr. Robert W. Boyle, Wauwatosa, Wis.; vice-president-elect, Dr. Louis B. Schwartz, Chicago; secretary-treasurer-elect, Dr. Bernard J. Michela, Chicago; and board of trustees-elect, Dr. Wladimir T. Liberson, Hines, Ill. These men will assume office Jan. 1, 1960.

Institute on Rehabilitation.—The sixth annual Institute for Rehabilitation Personnel will be conducted by the Rehabilitation Institute of Southern Illinois University, Carbondale, June 21-July 3. Special emphasis will be placed on a coordinated approach in the rehabilitation process. Co-sponsors of the institute, which is partially supported by a training grant from the Office of Vocational Rehabilitation, Department of Health, Education, and Welfare, are the Illinois Department of Public Welfare, Illinois Division of Vocational Rehabilitation, and the Illinois Tuberculosis Association. The program will consider the following topics:

The Scope of Rehabilitation.
Administrative Aspects of Rehabilitation.
The Rehabilitation Process.
Problems of the Handicapped.
Theory and Dynamics of Behavior.
Professional Responsibilities in Rehabilitation.
Sequences of Rehabilitation Services.
Pertinent Therapeutic Approaches in Rehabilitation.
Organizing Communities for Rehabilitation.

Enrollment fee is $55 and enrollment is limited to 60 persons. For information, write Guy A. Renzaglia, Ph.D., Director, Rehabilitation Institute, Southern Illinois University, Carbondale, Ill.

Chicago

Dr. Dragstedt Goes to Florida.—Dr. Lester R. Dragstedt, retired chairman of the department of surgery at the University of Chicago, will join the faculty of the University of Florida College of Medicine, Gainesville, as research professor of surgery, Aug. 1. At the University of Florida he will teach surgical physiology, basic physiology, and serve as counselor to resident physicians in surgery. Dr. Dragstedt introduced vagotomy in the treatment of peptic ulcer. His move to the University of Florida follows some 38 years' service at the University of Chicago where he was made full professor of surgery in 1930 and chairman of the department of surgery in 1948. Among his honors are the Certificate of Merit of the American Medical Association in 1937 for his original work on lipocaic; the appointment as lecturer of the Royal College of Surgeons of Canada in 1946; the Silver Medal of the American Medical Association in 1947; the appointment as honorary professor of surgery at the University of Guadalajara in 1953, and as honorary foreign member, Surgical Society of Lyon, France, in 1958.

Physicians are invited to send to this department items of news of general interest, for example, those relating to society activities, new hospitals, education, and public health. Programs should be received at least three weeks before the date of meeting.

LOUISIANA

Dr. Mickal Named Department Head.—Dr. Abe Mickal was named professor and head of the department of obstetrics and gynecology, Louisiana State University School of Medicine, New Orleans. Dr. Mickal will assume his duties July 1. He succeeds Dr. Milton L. McCall who will become medical director of the Elizabeth Steel Magee Hospital as well as chairman of the obstetrics and gynecology department at the University of Pittsburgh School of Medicine.

MINNESOTA

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NEW YORK

New York City

Dedicate Surgical Center.—A surgical center "designed exclusively for chronic disease treatment and research" was dedicated at St. Barnabas Hospital in the Bronx on May 13. Main speaker was Dr. Howard A. Rusk, director of the Institute of Physical Medicine and Rehabilitation, New York University-Bellevue Medical Center. The center, known as the Kane Surgical Addition, was constructed as an additional floor on the Kane Pavilion, an existing St. Barnabas building. The air-conditioned center consists of four operating rooms and supporting facilities. Largest among these is the neurosurgical operating room, which includes a wall-sized kymograph screen, visible from all part of the room, on which simultaneous recordings c the patient's blood pressure, pulse, respiration, an other measurements can be made. On a special "boom" that can be moved directly above the table, another monitor is located for recording visuall such measurements as electrocardiograms and electroencephalograms. Another "boom," which is movable over the table, contains a panel box with connections for thermostatically controlled warm ster saline; suction mechanisms; remotely controll electrocautery and electrocutting; x-ray contro timing devices and switches; electrostimulation co nections; and recorder connections.

The new chronic disease surgical center at St. Barnab Hospital located on top of Kane Pavilion (right).

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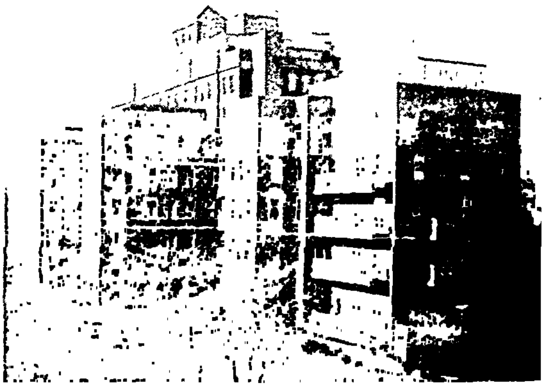

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Prevalence of Poliomyelitis.—According to the National Office of Vital Statistics, the following number of reported cases of poliomyelitis occurred in the United States, its territories and possessions in the weeks ended as indicated:

Area	May 23, 1959 Paralytic Type	May 23, 1959 Total Cases	May 24, 1958 Total
New England States			
Maine	..	..	..
New Hampshire	..	..	..
Vermont	..	..	..
Massachusetts	..	..	..
Rhode Island	..	..	..
Connecticut	..	..	..
Middle Atlantic States			
New York	..	..	..
New Jersey	..	..	..
Pennsylvania	..	..	..
East North Central States			
Ohio	2	5	1
Indiana	..	..	..
Illinois	..	..	..
Michigan	..	..	..
Wisconsin	..	..	..
West North Central States			
Minnesota	1	2	..
Iowa	..	..	1
Missouri	1	1	..
North Dakota	..	..	..
South Dakota	..	..	..
Nebraska	1	1	4
Kansas	..	1	..
South Atlantic States			
Delaware	..	..	..
Maryland	..	..	..
District of Columbia	..	..	..
Virginia	2	2	..
West Virginia	..	..	..
North Carolina	..	..	3
South Carolina	1	1	..
Georgia	1	1	..
Florida	4	5	2
East South Central States			
Kentucky	..	..	1
Tennessee	1	1	3
Alabama	..	..	..
Mississippi	..	..	..
West South Central States			
Arkansas	..	..	1
Louisiana	..	..	..
Oklahoma	..	1	..
Texas	7	9	9
Mountain States			
Montana	..	..	1
Idaho	..	..	..
Wyoming	..	..	..
Colorado	..	..	..
New Mexico	..	..	..
Arizona	5	5	..
Utah	..	..	1
Nevada	..	..	..
Pacific States			
Washington	..	1	..
Oregon	..	1	..
California	2	2	4
Alaska	..	..	..
Hawaii	..	..	1
Puerto Rico	..	..	2
Total	28	39	34

Request for Laboratory Quality Control Measures.—The Standards Committee of the College of American Pathologists urges that directors of all clinical pathology laboratories institute quality control measures as soon as possible in order to verify and certify the validity of measured results. Appropriate hniques are described by Freier and Rausch (Univ. Minn. Bull. 29:190, 1958). The Standards Committee of the College of American Pathologists (Prudential Plaza, Chicago 1) is willing to supply reprints of the above paper together with other information and assistance to anyone interested.

Mortality in Floods.—More than 2,400 persons lost their lives in floods in the United States in the past 30 years, according to statisticians of the Metropolitan Life Insurance Company. The loss of life since 1929 has varied from year to year, but the annual toll was generally less than 100. In 1931 no flood deaths whatever were reported. However, 302 lives were lost in 1955, the largest number for any year since 1927. Breaking the 30 years since 1929 into five-year periods, the heaviest loss of lives was in 1934-1938, when nearly 800 persons died in floods. During the 1954-1958 period, 555 such deaths occurred, reflecting mainly the catastrophes of the year 1955, when about two-thirds of the flood deaths occurred in the northeastern part of the country in floods resulting from the torrential rains accompanying the hurricane of Aug. 17-19. For the 30-year period as a whole, the Ohio Valley experienced a larger loss of life from floods than any other region, accounting for nearly a fourth of the victims in the entire country.

Increase in Paralytic Polio.—Almost twice as many cases of paralytic poliomyelitis have been reported during the first four months of 1959 as during the same period last year, Dr. John D. Porterfield, acting surgeon general, U. S. Public Health Service, announced. Dr. Porterfield pointed out that a 45% increase in paralytic polio occurred in 1958 over 1957 and urged a renewed vaccination effort. In the first week of May 19 new cases of paralytic polio were reported to the service as compared with only 7 for the same week in 1958. A total of 283 cases was reported so far in 1959 compared with 147 for the same period last year. At least 50 million persons in the high risk group—those under 40 years of age—have not been fully vaccinated, Dr. Porterfield pointed out. Surveys undertaken with Public Health Service assistance in Long Beach, Calif., Lexington, Ky., Columbus, Ohio, Denver, Washington, D. C., and Atlanta, Ga., all show that the larger percentage of the unvaccinated are in the lower socioeconomic groups. Substantial numbers of persons at all socioeconomic levels, however, still have not received the three shots of vaccine required for maximum protection, the service said.

Opportunities for Medical Officers.—The U. S. Civil Service Commission has announced opportunities for medical officers with the Federal Government in the United States and foreign countries at salaries from $7,510 to $12,770. Professional assignments are available in the following fields:

Administration; Anesthesiology; Cancer; Dermatology and Syphilology; Epidemiology; General Medicine and Surgery; Geriatrics; Internal Medicine; Maternal and Child Health; Nuclear Medicine; Nutrition; Obstetrics and Gynecology; Occupational Health and Medicine; Ophthalmology and Otorhinolaryngology; Pathology; Pediatrics; Pharmacology; Physical Medicine and Rehabilitation: Physiology; Preventive Medicine; Psychiatry and Neurology; Radiology; Surgery; Urology; and Venereal Disease.

An examination will be used to fill positions in various federal agencies in Washington, D. C., throughout the United States and its territories, and in foreign countries. The Federal Government employs about 1,100 medical officers with the following agencies as the major users of these officers: The National Institutes of Health; Army, Navy, and Air Forces installations; U. S. Public Health Service; St. Elizabeth's Hospital, Washington, D. C.; Indian Service Hospitals; Food and Drug Administration; and Children's Bureau. Officers conduct research, service as consultants, and investigate offenses and participate in the prosecution of violators of federal laws pertaining to foods, drugs, and cosmetics. Applicants must be graduates of a medical school of recognized standing, and for most positions must have completed an approved rotating internship, and be currently licensed to practice medicine and surgery in a state or territory. For positions in grades GS 12, applicants must have experience in the field in which they apply. Applicants must also show that they are citizens of the United States and physically able to do the work involved. For information write the U. S. Civil Service Commission, Washington 25, D. C.

CANADA

Sir Stewart Duke–Elder Honored.—Sir Stewart Duke–Elder, Ph.D., F.R.C.S., was awarded the Charles Mickle Fellowship for 1959 by the University of Toronto "for his outstanding research in ophthalmology." The Mickle Fellowship is the income from $29,000 bequeathed by the late Dr. W. J. Mickle and is awarded annually to the member of the medical profession who is considered by the Council of the University's Faculty of Medicine to have "done most during the preceding ten years to advance sound knowledge of a practical kind in medical art or science."

LATIN AMERICA

Congress on Physiological Sciences in Buenos Aires.—The 21st International Congress of Physiological Sciences (Physiology and Pharmacology) will be held at the Faculty of Medical Science in Buenos Aires, Argentina, Aug. 9-15. The program includes 12 symposiums, 16 special lectures, and 102 sessions in which 918 papers will be presented. Seventeen simultaneous meetings with nine papers each will be held each day. Simultaneous translations will be provided for special lectures and symposiums. Lectures delivered in English will be translated into Spanish and vice versa. Lectures delivered in French will be translated into English. For information write the Secretary, 21st International Congress of Physiological Sciences, Prof. A. O. M. Stoppani, Facultad de Medicina, Paraguay 2151, Buenos Aires, Argentina.

FOREIGN

Conference on Medical Electronics.—The second International Conference on Medical Electronics will be held at the new UNESCO Building in Paris, June 24-27. Activities will include general review sessions, symposiums, round-table discussions, scientific demonstrations, an exhibition, and a general business meeting. General subjects are planned as follows:

Diagnostic needs and aids in general practice.
Data processing (digital and analogue).
Electrophysiology.
Transducers.
Amplifiers.
Isotopes and radiology.
Instrument design (for reliability, simplicity, ease of maintenance and operation).

The official languages will be English and French, with translations available at the general sessions and symposiums. Membership fees are $9 for active members and $4 for associate members. For information write F. S. Brackett, Ph.D., National Institutes of Health, Bethesda 14, Md.

Joint British and Canadian Meeting.—The British Medical Association and the Canadian Medical Association will hold a joint annual scientific meeting July 20-24 in Edinburgh. Two plenary scientific sessions will be held at Edinburgh University the mornings of July 22 and 24. A general session will be held the morning of July 23. Twelve round-table conferences will be held at 9 a. m. on July 22, 23, and 24. A scientific exhibition and a medical art exhibition are planned, and a program of tours, golf, and ladies' entertainment is arranged. For information write Dr. D. P. Stevenson, Secretary, British Medical Association, Tavistock Square, London, W.C. 1.

International Course on Military Medicine.—An "international improvement course for young medical officers of the Health Services of all the armies of the world" will be given at Macolin (sport center of the Swiss Jura) Sept. 11-19. It is organized by the Health Service of the Swiss army, under the auspices of the International Committee of Military Medicine and Pharmacy with the cooperation of the International Committee of the Red Cross, the World Medical Association, and the World Health Organization. The program will be on the main principles of organization of the health services of the armies and on the general elements of army medicine, surgery, and hygiene. Lectures will be given on the main humanitarian principles which are at the basis of the practice of medicine in time of war. Registration for the course is free. The expenses of the sojourn amount to 10 Swiss francs per day. The course and sojourn are open to all medical officers (active and reserve) and to the doctors of the Red Cross societies who request it (number is limited to 100 students). For information, write to the "secrétariat-général du Comité *International de Médecine Militaire, Hôpital Militaire*, Liège, Belgium."

CORRECTIONS

Steel Company Donates Community Hospital.—In the March 7 issue of The Journal, page 1088, in Medical News, under this side head, the cost of the Hospital in the Pines should have been $500,000 instead of $30,000,000.

The Fertility Testor.—In the paper by Doyle and Ewers entitled "The Fertility Testor" (May 2, page 45) the statement in the opening paragraph that reads "Gluconic acid, the end-product, is converted to hydrogen peroxidase which, in the presence of traces of orthotolidine, produces a blue color that can be seen as shades of green when viewed on a yellow strip" should read "Glucose oxidase catalyzes the oxidation of glucose to gluconic acid. Hydrogen peroxide is a by-product, and, in the presence of peroxidase and an oxidizable dye such as orthotolidine, a color is produced."

EXAMINATIONS AND LICENSURE

MEDICAL SPECIALTY BOARDS

American Board of Anesthesiology: *Written.* Various locations, July 8, 1960. Final date for filing application is January 8. Sec., Dr. Forrest E. Leffingwell, 217 Farmington Ave., Hartford 5, Conn.

American Board of Dermatology: *Written.* Several Cities, Oct. 5. *Oral.* Oklahoma City, Jan. 15-18, 1960. The final date for filing all applications is July 1, 1959. Sec., Dr. Beatrice M. Kesten, One Haven Ave., New York 32.

American Board of Internal Medicine: *1959 Schedule—Written*, Oct. 19. Final date for filing application was May 1. *Oral.* For candidates on the West Coast, Portland, Ore., Sept. 9-12. Final date for filing application was March 1. *Oral.* For candidates on the East Coast, Nov. 6-7, 9-10. Final date for filing application was March 1. Sec.-Treas., Dr. William A. Werrell, One West Main St., Madison 3, Wis.

American Board of Neurological Surgery: Examination given twice annually, in the spring and fall. In order to be eligible a candidate must have his application filed at least six months before the examination time. Sec., Dr. Donald D. Matson, 300 Longwood Ave., Boston, Mass.

American Board of Obstetrics and Gynecology: Applications for certificates, new and reopened, Part I, and requests for re-examination Part II are now being accepted. All candidates are urged to make such application at the earliest possible date. Deadline date for receipt of applications is August 1, 1959. No applications can be accepted after that date. Sec., Dr. Robert L. Faulkner, 2105 Adelbert Road, Cleveland 6, Ohio.

American Board of Ophthalmology: *Oral.* Philadelphia, June 2-6; St. Louis, Oct. 6-10. *Written.* January 1960 in various cities. Applications for the 1960 written examination must be filed before July 1. Sec., Dr. Merrill J. King, Box 236, Cape Cottage Branch, Portland, Maine.

American Board of Orthopaedic Surgery: *Part II.* Chicago. Jan. 19-21, 1960. The deadline for the receipt of application is Aug. 15, 1959. Sec., Dr. Sam W. Banks, 116 South Michigan Ave., Chicago 3.

American Board of Otolaryngology: *Oral.* Chicago, Oct. 5-9. Final date for filing application was April 1. Sec., Dr. Dean M. Lierle, University Hospitals, Iowa City.

American Board of Pathology: New Orleans, Nov. 12-14. Final date for filing application is October 1. Sec., Dr. Edward B. Smith, Indiana University Medical Center, 1100 W. Michigan St., Indianapolis 7.

American Board of Pathology: *Examination in Forensic Pathology.* New Orleans, Nov. 13. Final date for filing application is October 1. Sec., Dr. Edward B. Smith, Indiana University Medical Center, 1100 W. Michigan St., Indianapolis 7.

American Board of Pediatrics: *Written.* January 1960. Exec. Sec., Dr. John McK. Mitchell, 6 Cushman Road, Rosemont, Pa.

American Board of Plastic Surgery: *Oral and Written.* Miami, Fla., Oct. 15-17. Final date for submitting case reports is July 1. Corresponding Secretary, Miss Estelle E. Hillerich, 4647 Pershing Ave., St. Louis 8, Mo.

American Board of Proctology: *Oral and Written.* Philadelphia, *September. Final date for filing application was* March 15. Sec., Dr. Stuart T. Ross, 520 Franklin Ave., *Garden City, N. Y.*

American Board of Psychiatry and Neurology: Chicago, Oct. 19-20; New York, Dec. 14-15; San Francisco, Mar. 14-15, 1960. Training credit for full time psychiatric and/or neurologic assignment in unapproved military programs or services between the dates of Jan. 1, 1950 and Jan. 1, 1954 was terminated on Jan. 1, 1959. Sec., Dr. David A. Boyd, 102-110 Second Ave. S. W., Rochester, Minn.

American Board of Radiology: *Examination.* Washington, Dec. 6-9. Deadline for filing application is July 1. Candidates examined in Diagnostic Roentgenology may expect to be examined in Physics. A Special Examination in Nuclear Medicine (for diplomates in Radiology or Therapeutic Radiology) was not given in June 1959. Candidates desiring this examination will be accommodated at the meeting of the Board in Washington, D. C. on December 5. Deadline for filing application is August 1. Sec., Dr. H. Dabney Kerr, Kahler Hotel Bldg., Rochester, Minn.

American Board of Surgery: *Written* examinations (Part I) will be held on December 2, 1959 at various centers to be announced later. Candidates are urged to apply several months before completion of training requirements although the closing date for filing applications is August 1. Those completing training requirements after September 30 cannot be considered for the Part I examination in December of the same year. Sec., Dr. John B. Flick, 1617 Pennsylvania Blvd., Philadelphia 3.

Board of Thoracic Surgery: *Written.* Various centers throughout the country, September 1959. Final date for filing application is July 1. *Oral.* September. Final date for filing application is July 1. Sec., Dr. William M. Tuttle, 1151 Taylor Ave., Detroit 2, Mich.

American Board of Urology: *Written.* Approximately 25 cities throughout the country, December 4, 1959. *Oral-Clinical* and *Examination in Pathology.* Chicago, February 1960. Final date for filing application is Sept. 1, 1959. Sec., Dr. William Niles Wishard, 30 Westwood Rd., Minneapolis 26, Minn.

DEATHS

Bandler, Leon S., Coronado, Calif.; Columbia University College of Physicians and Surgeons, New York City, 1900; died in the Coronado Hospital March 20, aged 87.

Barnhill, James E. Ⓜ Owensboro, Ky.; Hospital College of Medicine, Louisville, 1898; member of Aero Medical Association, served on the board of directors of the Owensboro Federal Savings and Loan Association; on the courtesy staff of Owensboro–Daviess County Hospital, where he died March 30, aged 81.

Bess, Thomas Floyd Ernest Ⓜ Keyser, W. Va.; born in 1890; College of Physicians and Surgeons, Baltimore, 1914; member of the Southeastern Surgical Congress; fellow of the American College of Surgeons; past-president and vice-president of the West Virginia State Medical Association; served a term as president of the Potomac Valley Medical Society; veteran of World War I; a member of the executive committee of the Boy Scouts of America and was awarded the Silver Beaver in scouting; past-president of the Keyser Rotary Club and a past-district-governor of the 180th Rotary District; served as medical superintendent of the Potomac Valley Hospital, which he and his brother built; died at his summer cottage near Aurora March 18, aged 68.

Bowser, Herschel Philip, Goshen, Ind.; Indiana University School of Medicine, Indianapolis, 1921; died March 28, aged 63.

Buckner, Hubbard Thomas Ⓜ Seattle; born in Hazleton, Pa., Aug. 17, 1889; Jefferson Medical College of Philadelphia, 1913; fellow of the International College of Surgeons and the American College of Surgeons; member of the American Association for the Surgery of Trauma; veteran of World War I; during World War II organized and commanded the 50th General Hospital and was awarded the Bronze Star for distinguished service in Normandy; member of the board of regents of Seattle University which in 1950 recognized his services with the military hospital group and awarded him an honorary degree of doctor of laws; associated with Providence, Doctors, King County, and United States Public Health Service hospitals; medical director of the Washington State Rehabilitation Center of the Department of Labor and Industries since 1948; the new center, named in his honor, was dedicated Feb. 21, 1959; died March 22, aged 69.

Carlton, Arthur J. Ⓜ Escanaba, Mich.; University of Michigan Department of Medicine and Surgery, Ann Arbor, 1904; past-president of the Delta-Schoolcraft County Medical Society; past-president of the Escanaba Board of Education; served for many years as health officer; on the staff of St. Francis Hospital, where he died March 31, aged 78.

Cerchiara, Camillo Anthony Ⓜ Mount Vernon, N. Y.; Cornell University Medical College, New York City, 1922; veteran of World War I; founding fellow of the American College of Obstetricians and Gynecologist; for many years on the staff of the staff of the Mount Vernon Hospital; died March 26, aged 62.

Clapsaddle, Clare Jury Ⓜ Ste. Genevieve, Mo.; St. Louis University School of Medicine, 1917; veteran of World War I; died in Firmin Desloge Hospital, St. Louis, March 14, aged 68.

Clark, Ira Joseph Ⓜ Vista, Calif.; Denver and Gross Medical College, 1908; veteran of World War I; served on the staff of the Oceanside (Calif.) Hospital; died in Fall Brook (Calif.) Community Hospital March 5, aged 83.

Cochran, Carlisle Calahan Ⓜ Kimball, W. Va.; Medical College of Virginia, Richmond, 1921; past-president of the McDowell County Medical Society; veteran of World War I and was awarded the Congressional Medal of Honor; on the staff of the Stevens Clinic Hospital in Welch, where he died March 24, aged 65.

Cooke, Quinton H., Rich Square, N. C.; University of North Carolina School of Medicine, Chapel Hill, 1905; died in the Roanoke–Chowan Hospital in Ahoskie, March 31, aged 79.

Coultas, Porter Jasper Ⓜ Tell City, Ind.; University of Louisville (Ky.) Medical Department, 1909; veteran of World War I; during World War II the examining officer for the Perry County Selective Service; county health officer and county coroner; served as city health officer; associated with the Protestant Deaconess and St. Mary's hospitals in Evansville, and Perry County Memorial Hospital; for many years a director of the Citizens National Bank, where he served for a period as vice-president; past-president of the Tell City Chamber of Commerce; died in the Veterans Administration Hospital in Louisville, Ky., March 20, aged 76.

Davies, Rupert Arthur Ⓜ Arlington, Neb.; Rush Medical College, Chicago, 1900; also a pharmacist; served on the village and school boards, and as

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Ⓜ Indicates Member of the American Medical Association.

mayor of Arlington; local surgeon with the Chicago and Northwestern Railway; past-president of the Dodge County Medical Society and the Elkhorn Valley Medical Society; a director of the Arlington Bank; on the staff of the Dodge County Community Hospital in Fremont, where he died March 20, aged 84.

Estabrook, Charles Taylor Ⓜ Worcester, Mass.; Long Island College Hospital, Brooklyn, 1897; past-president of the Worcester Eye, Ear, Nose and Throat Society; served on the staffs of the Fairlawn, Hahnemann, and St. Vincent hospitals; on the staffs of the Memorial Hospital and the Worcester City Hospital, where he died March 21, aged 86.

Fast, Ralph Bryan Ⓜ Kalamazoo, Mich.; University of Michigan Medical School, Ann Arbor, 1922; served on the faculty of his alma mater; specialist certified by the American Board of Otolaryngology; member of the American Academy of Ophthalmology and Otolaryngology; past-president of the Kalamazoo Academy of Medicine; associated with Borgess and Bronson Methodist hospitals; veteran of World War I; a member of the board of directors of the First National Bank; died March 24, aged 61.

Fox, John Francke Ⓜ Bluefield, W. Va.; University of the City of New York Medical Department, New York City, 1886; once served as a member of the city council; fellow of the International College of Surgeons and the American College of Surgeons; a division surgeon for the Norfolk and Western Railway; in 1946 presented the city's Distinguished Citizenship Award in recognition of his many contributions; member of the surgical staff and one of the founders of the Bluefield Sanitarium, where he was for a long time its president and senior surgeon, and where he died April 4, aged 95.

Franklin, Earl Alexander Ⓜ San Francisco; Jefferson Medical College of Philadelphia, 1922; veteran of World War II; died in St. Francis Hospital Feb. 14, aged 63.

Friedland, Henry Ⓜ New York City; University and Bellevue Hospital Medical College, New York City, 1911; past-secretary of the Bronx County Medical Society; specialist certified by the American Board of Radiology; member of the American College of Radiology; radiology consultant at the Hebrew Home and Hospital for Chronic Sick; attending physician and a member of the medical board at the Home and Hospital of the Daughters of Jacob; served as a director of radiology at Kew Gardens (N. Y.) General Hospital; died March 30, aged 70.

Geen, James S., Utica, Ill.; Baltimore Medical College, 1896; also a graduate in pharmacy; for many years associated with the La Salle County Tuberculosis Sanatorium in Ottawa, where he was president of the board of directors; on the staff of St. Mary's Hospital in La Salle; died in St. Petersburg, Fla., March 7, aged 88.

Greiner, Theodore Ⓜ University City, Mo.; Washington University School of Medicine, St. Louis, 1897; past-president of the St. Louis Dermatological Society; member of the American Academy of Dermatology and Syphilology; associated with St. Louis County Hospital, St. John's Hospital, and De Paul Hospital, where he died March 30, aged 84.

Herzberg, Mortimer Jr., Hillsboro, Ohio; University of Cincinnati College of Medicine, 1939; veteran of World War II; served as health commissioner of Highland County; on the staff of the Highland Community Hospital; died in the Veterans Administration Hospital, Cincinnati, March 17, aged 47.

Higgins, Thomas Joseph Ⓜ Baker, Ore.; Creighton University School of Medicine, Omaha, 1906; member of the American Academy of General Practice; veteran of World War I; served on the state board of health; on the staff of St. Elizabeth Hospital, where he died March 19, aged 77.

Holmes, George Winslow Ⓜ Belfast, Maine; born in Waldo, Maine, Dec. 28, 1876; Tufts College Medical School, Boston, 1906; specialist certified by the American Board of Radiology; since 1941 clinical professor of roentgenology emeritus at Harvard Medical School in Boston, where he joined the faculty in 1913 as assistant in roentgenology, subsequently serving as instructor in roentgenology, assistant professor, and clinical professor; member and in 1924 president of the American Roentgen Ray Society; in 1940 received the Caldwell Medal, following his delivery of the Caldwell Lecture; served as a director of the American Society for the Control of Cancer and a member of the National Research Council; for many years associated with the Massachusetts General Hospital in Boston, where he served as chief roentgenologist; served as consulting roentgenologist for the Massachusetts Eye and Ear Infirmary in Boston; on the staff of the Waldo County General Hospital; the *American Journal of Roentgenolgy and Radium Therapy* devoted an entire edition in honor of him in December, 1936; joint author of "Roentgen Interpretation"; died March 18, aged 82.

Janis, Lee Davidson Ⓜ Brooklyn; New York University College of Medicine, New York City, 1940; specialist certified by the American Board of Preventive Medicine; service terminated with the U. S. Public Health Service Nov. 11, 1947; associated with New York Hospital–Cornell Medical Center; member of the medical department of the advertising firm of William Douglas McAdams in New York City, and consultant to World Wide Medical News Service; died in the Long Island College Hospital March 26, aged 43.

Johannesen, Robert Eastnor Ⓜ Altadena, Calif.; Rush Medical College, Chicago, 1928; veteran of World War I; associated with St. Luke Hospital and the Alta Vista Hospital in Pasadena; died April 2, aged 61.

Lewis, George Andrew, Chicago; Howard University College of Medicine, Washington, D. C., 1899; associated with the Provident Hospital; died April 6, aged 83.

McCormac, James Francis, Verona, Ky.; Medical College of Ohio, Cincinnati, 1895; died in St. Elizabeth Hospital, Covington, Feb. 10, aged 87.

Mackowsky, Edwin L. Ⓜ Jersey City, N. J.; Eclectic Medical College, Cincinnati, 1939; veteran of World War II, and was decorated with the Bronze Star; associated with the Medical Center of Jersey City, St. Francis Hospital, Margaret Hague Maternity Hospital, and Christ Hospital; died March 23, aged 44.

Marks, Edward Schaefer Ⓜ Marietta, Ga.; Emory University School of Medicine, Atlanta, 1943; specialist certified by the American Board of Surgery; fellow of the American College of Surgeons; veteran of World War II; interned at the Cincinnati General Hospital; served a residency at the Veterans Administration Hospital in Memphis, Tenn.; named "Young Man of the Year" in 1953; on the staff of the Kennestone Hospital; died in Lake George, Fla., aged 40.

Maryan, Harry Oliver Ⓜ Chicago; University of Illinois College of Medicine, Chicago, 1924; specialist certified by the American Board of Obstetrics and Gynecology; member of the Central Association of Obstetricians and Gynecologists; fellow of the International College of Surgeons; affiliated with American, Forkosh, Frank Cuneo Memorial, and Augustana hospitals, and the Columbus Hospital, where he died March 28, aged 63.

Matlock, John William, Frost, Texas; University of Texas School of Medicine, Galveston, 1901; died March 14, aged 86.

Miller, Charles Arthur Ⓜ Macon, Ill.; College of Physicians and Surgeons of Chicago, School of Medicine of the University of Illinois, 1902; Macon townspeople honored him for 50 years practice in the vicinity with a "Dr. Miller Day" on June 18, 1952; died March 21, aged 83.

Moseley, Harry Gladding Ⓜ Colonel, U. S. Air Force, Denver, Colo.; born in Roanoke, Va., Dec. 1, 1908; Washington University School of Medicine, St. Louis, 1938; appointed a first lieutenant in the Army of the United States June 7, 1938; reported for active duty July 5, 1939; commissioned a first lieutenant in the U. S. Army on Feb. 14, 1940; transferred to the United States Air Force on July 1, 1949; member of the Aero Medical Association and received its Theodore Lyster Award at the 1958 meeting in Washington for developing a successful program in the aeromedical aspects of aircraft accident prevention; his military decorations included the Air Force Commendation Ribbon; died near Norton Air Force Base, Calif., where he was assigned to 1002d Inspector General Group, Feb. 10, aged 50.

Moshinsky, Alexander L., New York City; University of St. Vladimira Faculty of Medicine, Kiev, Russia, 1922; specialist certified by the American Board of Otolaryngology; member of the American Academy of Ophthalmology and Otolaryngology; fellow of the American College of Surgeons; served on the staffs of the Beth Israel, Gouverneur, Good Samaritan, Trinity, Beth David, and New York Post-Graduate Medical School and hospitals; died in the Phelps Memorial Hospital, North Tarrytown, March 25, aged 63.

Moursund, Walter Henrik Sr., Houston, Texas; born in Frederickburg, Aug. 13, 1884; University of Texas School of Medicine, Galveston, 1906; joined the faculty of Baylor University College of Medicine in 1911 as assistant in pathology and bacteriology, subsequently becoming professor of physiology, professor of pathology and bacteriology, secretary and registar, professor of pathology, professor of bacteriology, professor of clinical pathology, professor of bacteriology and hygiene, professor of hygiene and preventive medicine, acting dean, dean, and since 1953 dean emeritus; served as captain and major, medical reserve corps, U. S. Army, becoming a member in 1910; during World War I commanded the Eighth Corps Area Laboratory at Fort Sam Houston; a charter member of the board of directors of Baylor Medical Foundation; in 1944 awarded an honorary LL.D. degree from Baylor University; wrote "A History of Baylor University College of Medicine—1900-1953"; died in the Methodist Hospital April 2, aged 74.

Mulherin, Francis Xavier Ⓜ Augusta, Ga.; University of Pennsylvania School of Medicine, Philadelphia, 1911; veteran of World War I; in 1958 was named "Doctor of the Year" by the Richmond County Medical Society and shortly after was chosen "General Practitioner of the Year" by the Medical Association of Georgia; on the staffs of University and St. Joseph's hospitals; died March 14, aged 73.

Nolte, Albert E. Ⓜ Weirton, W. Va.; College of Physicians and Surgeons, Baltimore, 1908; served as city health officer at Benwood; an honorary staff member of the Ohio Valley General Hospital in Wheeling; died in Steubenville, Ohio, March 16, aged 76.

O'Brien, Kennedy William Ⓜ Lynbrook, N. Y.; Loyola University School of Medicine, Chicago, 1941; member of the American Academy of General

Practice; veteran of World War II; on the staffs of the Mercy Hospital and the South Nassau Communities Hospital in Rockville Centre; died in the Veterans Administration Hospital in Fort Hamilton, Brooklyn, March 20, aged 44.

O'Brien, Minnie Carrie Ⓜ San Antonio, Texas; Woman's Medical College of Pennsylvania, Philadelphia, 1906; formerly vice-president of the Bexar County Medical Society; served as vice-president of the Texas Association of Obstetricians and Gynecologists; on the staff of the Robert B. Green Memorial Hospital; died March 12, aged 74.

Price, Robert L., Jackson, Miss.; Louisville (Ky.) Medical College, 1892; died March 29, aged 90.

Rosenbluth, Milton Benjamin Ⓜ New York City; Columbia University College of Physicians and Surgeons, New York City, 1914; specialist certified by the American Board of Internal Medicine; professor of clinical medicine at the New York University College of Medicine; at one time on the faculty of Fordham University School of Medicine; veteran of World War II; served on the staffs of the Harlem Hospital, New York University division of Bellevue Hospital, and the Goldwater Memorial Hospital; died in the Doctors Hospital March 23, aged 68.

Sayre, Bernard Edward Ⓜ Chicago; University of Illinois College of Medicine, Chicago, 1924; associated with Mount Sinai and Walther Memorial hospitals; died in the Louis A. Weiss Memorial Hospital March 30, aged 59.

Stephens, Perry A., Chattanooga, Tenn.; Knoxville Medical College, 1907; served on the staff of the Carver Memorial Hospital; died March 3, aged 75.

Stokes, William Ellis, Downey, Calif.; Baltimore Medical College, 1913; died in the Presbyterian Hospital–Olmsted Memorial in Los Angeles March 1, aged 73.

Trask, Leo Stewart Ⓜ Everett, Wash.; Johns Hopkins University School of Medicine, Baltimore, 1913; member of the American Association for the Surgery of Trauma; fellow of the American College of Surgeons; served in the regular Army and during World War I; associated with General and Providence hospitals; died March 16, aged 73, of coronary disease.

Vogel, Julius Aloysius Ⓜ Monaca, Pa.; University of Pittsburgh School of Medicine, 1927; specialist certified by the American Board of Preventive Medicine; member of the Industrial Medical Association; plant physician at the Aliquippa Works, Jones and Laughlin Steel Corporation; on the staff of the Aliquippa (Pa.) Hospital; died in Cleveland March 11, aged 57.

Walker, Glen Ⓜ Farina, Ill.; Loyola University School of Medicine, Chicago, 1928; veteran of World War I; affiliated with the Fayette County Hospital, Vandalia; died March 20, aged 60.

Weaver, William Jackson Ⓜ Asheville, N. C.; Jefferson Medical College of Philadelphia, 1898; died Feb. 8, aged 85.

White, George Washington, Richmond, Va.; Howard University College of Medicine, Washington, D. C., 1913; served as president of the Federal Life Insurance Company of Washington; vice-president of the Richmond Beneficial Life Insurance Company, of which he was medical director; associated with the Richmond Community Hospital; member of the courtesy staff of Richmond Memorial Hospital; died Feb. 15, aged 74.

Wiley, A. Ray Ⓜ Tulsa, Okla.; University of Oklahoma School of Medicine, Oklahoma City, 1913; fellow of the International College of Surgeons and the American College of Surgeons; past-president of the Tulsa County Medical Society; for ten years a member of the city-county board of health; served in the Oklahoma National Guard during World War I and was a captain in the medical corps when it was deactivated in 1919; served on the staff of the Hillcrest Medical Center, where he died March 13, aged 68.

Wilkinson, William Emmet, Alexandria, La.; Maryland Medical College, Baltimore, 1910; veteran of World War I; served on the staffs of the East Louisiana State Hospital in Jackson, and State Colony and Training School in Pineville; affiliated with the Veterans Administration Hospital in Alexandria; died Feb. 27, aged 70.

Wilson, George Ⓜ Philadelphia; University of Pennsylvania School of Medicine, Philadelphia, 1911; specialist certified by the American Board of Psychiatry and Neurology; served on the faculty of his alma mater and the Woman's Medical College of Pennsylvania; member of the American Neurological Association, of which he was past-president, and the American Academy of Neurology; fellow of the American Psychiatric Association; veteran of World War I; associated with Bryn Mawr (Pa.) Hospital, Methodist Episcopal Hospital, Episcopal Hospital, in Philadelphia, Thomas M. Fitzgerald Mercy Hospital in Darby, Pa., State Hospital, Norristown, and the Pennsylvania Epileptic Hospital and Colony Farm in Oakbourne, Pa.; president of the Fairmount Farm; formerly consultant for the U. S. Public Health Service; died March 23, aged 70.

Wright, Ray Barkley Ⓜ Laredo, Texas; Physio-Medical College of Indiana, Indianapolis, 1897; served with the U. S. Public Health Service; veteran of World War I; for many years a pharmacist; died in the Mercy Hospital March 10, aged 84.

FOREIGN LETTERS

DENMARK

Rectopexy for Rectal Prolapse.—H. Baden and O. Mikkelsen (*Acta chir. scandinav.* 116:230-234, 1958/1959) reported on 33 patients (27 women and 6 men) with complete rectal prolapse in whom the rectum was mobilized deeply in the pelvis and fixed to the promontory after elevation. The ages of the patients ranged from 24 to 80 (average 58) years. The disease had persisted from 3 months to 35 years, and at least 5 patients had had the condition for over 10 years. There was one operative death, a woman aged 72 who died four days after operation for a pulmonary embolus. Thirty patients were examined from two months to seven years after the operation. There was one recurrence, and four patients had a small mucosal prolapse. Only two patients suffered from incontinence. The authors concluded that rectopexy after mobilization of the rectum was one of the best and least radical operations for complete rectal prolapse in adults.

Fractures of the Femur in the Elderly.—T. Budtz-Olsen and A. Pahl (*Nord. med.* 61:360-362 [Feb. 26] 1959) reported a series of 114 patients over the age of 70 with fracture of the femoral neck, whom they divided into three risk groups on the bases of cardiopulmonary, urologic, and cerebral conditions. The study indicated that in the two groups of good-risk patients osteosynthesis should be considered the preferred operation. In the poor-risk group treatment by intermittent traction was tried in an attempt to lower the death rate at the expense of a good functional result. It was found, however, that this treatment did not influence mortality and hence that osteosynthesis might be used in this group too, although a high death rate could not be avoided in the physically weaker patients.

Fractures of the Femur in Children.—B. Barford and J. Christensen (*Acta chir. scandinav.* 116:235-250, 1958/1959) reported the results of a follow-up study of fractures of the femoral shaft in 114 children (86 boys and 28 girls) under 15 years of age, treated in two hospitals in Aarhus. The observation periods ranged from 2 to 12 years. The incidence of fractures was highest in the 3rd year of life and then fell with increasing age. Osteosynthesis was performed only in patients over 3 years of age. Fractures of the right and the left femur were equally common. Osteosynthesis was used in 23 cases and conservative treatment in 91. The duration of treatment was longer for osteosynthesis than for conservative treatment. The overgrowth of the injured limb after conservative treatment seemed to bear a direct relationship to the shortening observed at discharge, which suggested that a desirable compensation occurred. Of the fractures treated conservatively about 80% showed normal length ± 1 cm. at the follow-up examination. After osteosynthesis overgrowth always occurred as compared with the uninjured limb. Follow-up examination revealed lengthening in excess of 1 cm. in 20 of 23 patients. Shortening of at most 2 cm., angulation of less than 25 degrees, and absence of rotation should be the therapeutic goals. These may always be attained by conservative treatment, and the authors concluded that osteosynthesis of fracture of the femoral shaft in children was not indicated.

Ulcerative Colitis.—In *Acta chirurgica scandinavica* (supp. 236, 1958, pp. 1-118) Lindenberg assessed the results of medical and surgical treatment of ulcerative colitis in 161 patients. The medical series consisted of 87 patients whose average age at the onset of the disease was 30 years; 72% developed complications in the course of the disease. As 23% of the patients were operated on for this disease, the series was divided into a purely medical group of 67 patients and a medicosurgical group of 20. There was no difference in principle between the two groups with regard to age, sex, onset, and duration of the disease. All the patients were given diatetic treatment. Most of them were given rectal enemas and chemotherapeutic agents, some were treated with antibiotics, and a few received ACTH and cortisone. A body weight less than 80% of the ideal during the disease appeared to be a bad prognostic sign. A high or septic temperature and a pulse rate exceeding 120 per minute occurred only in those patients who died of the disease.

The death rate in the purely medical group was 30% with an average duration of illness for the dead of 5 years and four months and an average age at death of 38 years. Of the 67 patients 21% died before the age of 40. A follow-up study of 47 patients revealed that 19% were fully fit to work, 51% had diminished working capacity or were incapacitated, and 30% had died by the time of the study. In the medicosurgical group 11 patients had appendicostomy and colostomy and 10 patients had an ileostomy with or without subtotal colectomy. Appendicostomy and cecostomy had no effect. Colostomy and

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The items in these letters are contributed by regular correspondents in the various foreign countries.

ileosigmoidostomy resulted in a stormy postoperative course with no change in the symptoms or in the death rate. Ileostomy with subsequent resection proved fatal in seven, and the mortality in the whole medicosurgical group was 60%.

At the time of the follow-up study only three patients with ileostomy were symptom-free and five patients who had other operations had symptoms of ulcerative colitis either continuously or when working. The surgical series comprised 74 patients, including an American group of 55 and a Danish group of 19. All the patients were subjected primarily to ileostomy. The average ages at onset of the disease in the two surgical groups were practically identical, 29 years; 95% of the Danish and 81% of the American patients had complications of the disease. In the American series the technique of the ileostomy was that of bringing out the ileum in the incision without suturing. In the Danish series ileostomy was performed with a tunnel-shaped excision of the abdominal wall in 15 of the patients, omitting suture between the intestine and the wall, a technique devised by the author. Dysfunction of the ileostomy occurred in 60% of the American and in none of the Danish patients.

The author concluded that the purely medical and the two surgical series were sufficiently uniform to allow an evaluation of the efficacies of the different forms of treatment. The treatment should be primarily medical, although no specific medical treatment could be recommended. Medical treatment gave full work capacity in 19% after prolonged treatment and a mortality of 30%, within an average observation period of 12½ years. The prognosis was bad for patients in whom the disease had an acute onset. The general clinical symptoms afforded the best guidance to therapy and prognosis, whereas the results of proctoscopy, fluoroscopy, and laboratory studies were of questionable prognostic value. The indications for surgical treatment comprise absolute and relative indications. In the surgical series the patients who survived ileostomy and subsequent resections attained full work capacity after a short time. The operative mortality was 27% in the American and 21% in the Danish series. With use of the surgical technique described by the author ileostomy dysfunction, the most frequent and most difficult postoperative complication to treat, was avoided. Other operations than ileostomy, subtotal colectomy, and removal of the rectum generally have no effect on ulcerative colitis. Ileostomy and subtotal colectomy performed in two stages presumably cause fewer deaths than one-stage operations.

Cortisone for Rheumatoid Arthritis.—Leif Nyros (*Acta rheumatol. scandinav.* 4:225-242, 1958) reported a series of 148 patients (36 men and 112 women) all of whom received prolonged treatment with cortisone for rheumatoid arthritis and 67% of whom were over 50 years of age. The series consisted of patients for whom other treatment, particularly with sodium gold thiosulfate, had failed, and most were severely affected. The average duration of the disease was 11½ years. Long-term treatment with cortisone gave satisfactory results in 34% but it was stopped in 38% of these because of side-effects, and 28% became refractory to the treatment sooner or later. The mortality was the same as with conservative treatment. Only one of the deaths could be directly ascribed to cortisone, but it was a possible contributory factor in three deaths. It may be assumed that treatment with cortisone or other steroids permits a reduction in the speed of progress of the disease and delays the onset of irreversible lesions.

Subcutaneous Rupture of Quadriceps Femoris Tendon.—A follow-up study of 18 patients with 19 ruptures of the quadriceps femoris tendon was made by E. Jensen and P. Kølle-Jørgensen (*Nord. med.* 61:364-368 [Feb. 26] 1959). All patients were elderly, heavily built men. The most frequent cause of rupture was a fall on the knee in hyperflexion. The diagnosis was often overlooked for some time after the accident. In most patients a good result was obtained by primary suture of the ruptured tendon. Six of the patients were treated with suture, combined with grafting of the fascia lata and early mobilization, whereas 12 were treated with suture alone and prolonged immobilization in plaster. The end-result and the period of restitution were the same in the two groups. In these patients the prognosis seemed to be unaffected by a late diagnosis and operation.

INDIA

Frequent Coughs and Colds.—G. Coelho (*Indian Journal of Child Health,* vol. 8, March, 1959) in an analysis of 300 children with frequent coughs and colds attending a private clinic found that about half of them were under the age of 3 years. There was a noticeable decline after the 5th year. The frequency of these attacks varied from once a fortnight to twice a year. Cough associated with cold was the commonest complaint, being present in 173 patients. A congested throat was observed in 102; enlarged tonsils in 95; and rhonchi, rales, crepitations, and prolonged expiration in 98. Fluoroscopy showed hilar shadows in 34 and opacities in 4. Leukocytosis was present in 204 patients. The duration of symptoms ranged from two months to five years. The attacks started after whooping cough in seven, measles in two, and chickenpox, diphtheria, and influenza in one each. Some children had a history of measles or whooping cough after the commencement of attacks of coughs and cold; the latter were not aggravated during the acute illness. A history of food allergy could be elicited in many children, the articles of food which brought on the attack being ice cream, buttermilk, lime juice, banana, and peppermint.

Some of the patients had repeated bacterial or viral infections of the upper respiratory tract. This group had a better prognosis and was more amenable to treatment, as antibiotics were of great help in these cases. Penicillin and streptomycin were given patients with polymorphonuclear leukocytosis, while the broad-spectrum antibiotics were used for those showing lymphocytic leukocytosis. These were given for eight days every month for six months. Children with an eosinophil count above 500 per cubic millimeter were given a piperazine derivative and either carbarsone by mouth or injections of acetylarsan. Better results were obtained with acetylarsan. For children with only a cough and cold therapy with an antihistamine with a combination of acetophenetidin, aspirin, and codeine was prescribed and the nasal passages were kept clear with an ephedrine or hydrocortisone solution. Antihistaminics were prescribed twice a day for six months as prolonged administration of these drugs was found to increase the intervals between attacks. Tonsillectomy was performed on four patients, after which only one showed improvement.

Enterocolitis in Children.—D. F. Dauis-Lawas (*Indian Journal of Child Health*, vol. 8, March, 1959) stated that diarrhea in children is very common in the tropics, being even more prevalent than bronchopneumonia and tuberculosis. This is also true for deaths from these causes. Death may be due to toxemia (which was seen to occur in well-nourished as well as poorly nourished infants), dehydration, or secondary infections. In a series of about 6,000 children admitted to hospital with diarrhea intra-abdominal complications necessitating immediate operation occurred in 12. Of these 10 died and autopsies were performed on all; one was taken from the hospital against medical advice after operation, and one on whom operation was performed early survived. These complications included volvulus; intussusception; massive hemorrhage; and intestinal obstruction due to atony, perforation with peritonitis, gangrene, and liver abscess. Sudden cessation of the diarrhea was striking and occurred in four cases. Three of these had developed peritonitis with ileus and one had developed volvulus.

Hodgkin's Disease in Children.—M. V. Sirsat (*Indian Journal of Child Health*, vol. 8, March, 1959) stated that the diagnosis of enlarged lymph nodes in a child can prove difficult, as there may be no clear-cut clinical difference between such conditions as tuberculous lymphadenitis, Hodgkin's disease, lymphosarcoma, lymphoepithelioma, or even metastatic carcinoma. Reliance then must be placed on microscopic examination, which will also decide the line of treatment and the prognosis. A series of 1,640 lymph nodes were examined microscopically in the Tata Memorial Hospital, Bombay, between 1941 and 1957 in patients who were admitted with a clinical diagnosis of primary malignant neoplasm of the lymph node. This was confirmed by histological examination in only 25% of the patients. Of these 11% were children under 14 years of age. A total of 208 cases of Hodgkin's disease were recorded in the laboratories of this hospital in the same period, of which 50 were in patients under 14 years of age. The final diagnosis in every case was made by histological examination. The youngest patient in this series of 50 was 4 years old, most cases being found in children aged from 9 to 13 years (in adults the largest number was seen in the age group 21 to 30 years).

The preponderance in boys was remarkable (48 of the 50). The lymphatic enlargement was painless. Clinically the three types of involvement seen were cervical adenopathy, combined cervical and inguinal adenopathy, and generalized adenopathy. Axillary or inguinal lymph nodes alone were rarely involved. The common complaints besides swelling of lymph nodes were weakness, fatigue, loss of weight, and fever. The average duration of symptoms before hospitalization was nine months. The spleen was palpable in 32% of the patients and the liver in 18%, but none had jaundice. Almost all patients showed a steadily progressive hypochromic anemia; 56.6% had a leukocyte count above 8,000 per cubic millimeter. Eosinophilia (5% or more) was found in only 26% of the patients. A marked preponderance of Hodgkin's sarcoma was found in children compared to adults, the incidence being 12% in children and 5.6% in adults.

Statistical Survey of Tuberculosis.—S. D. Soman (*Journal of the Association of Medical Women in India*, vol. 47, February, 1959) stated that of more than 80 million persons in India who were tested with tuberculin 45% gave positive reactions, while the infection rate per year was 5%. Thus more than half of the population may still be infected. The percentage of positive tuberculin reactions was higher in large towns than in villages, and this difference was more obvious in children under the age of 6 years. The rate of positive reactions in small towns and villages approximated that of large towns in persons between the ages of 15 and 25 years. Antenatal roentgenograms of 173 women showed that 29 had evidence of infection—a higher percentage than that obtained by tuberculin testing. Roentgenograms of strongly positive tuberculin reactors and their contacts showed positive findings in 13% of the males as compared to 17% of the females.

In persons between the ages of 10 and 30 years the morbidity in males was 11% and in females 19%. The total mortality was higher in males than in females, and the death rate from tuberculosis in different age groups showed a constant variation as seen from curves plotted for the years 1900, 1932, and 1940. The total death rate was reduced over this period, however, thus showing that some constant factor is probably responsible for maintaining this peculiar distribution of mortality in different age groups. The death rate in boys and girls up to the age of puberty showed little difference, but after that age the female death rate rose above that for males and remained at a higher level for some time, then came down to a level below that of the males and remained at a lower level until old age, when they again became nearly equal.

In women of childbearing age the death rate rose sharply, with a peak between the ages of 20 and 30 years. An abrupt rise in the death rate from tuberculosis after childhood and coinciding with the onset of puberty was also noticed, and this rise occurred earlier in the females than in the males. Childbearing is generally supposed to be hazardous for the tuberculous woman and labor to have a deleterious effect on tuberculosis. If all the deaths due to tuberculosis in young women that were associated with pregnancy within a year of the onset of symptoms were subtracted from the total deaths due to tuberculosis in this age period, the difference between the death rates in young men and women would be far less conspicuous. Thus childbearing constitutes a sex-determined potential hazard, necessitating control of the activity of the disease even before conception occurs. Therapy alone is not enough to reduce the death rate in women of childbearing age.

Lymphogranuloma Venereum.—N. Krishnamurthi (*Antiseptic*, vol. 56, March, 1959) treated 10 patients who had lymphogranuloma venereum with sulfamethoxypyridazine. Patients with buboes attending the venereal disease clinic with no apparent sores and a positive result of the Frei test were selected for this trial. The dosage schedule was one tablet twice a day on the first day and one tablet daily for five or six days, a total dosage of seven or eight tablets per patient. All the patients were men between 20 and 30 years of age and all had unilateral buboes. The duration of the inguinal swelling varied from one to four weeks. Only one patient had fever with urticarial rash all over his body.

As a result of treatment pain and tenderness over the bubo subsided within 48 to 72 hours of starting therapy with the drug. In six patients the buboes disappeared completely while in the rest they became fluctuant and were aspirated. No residual buboes were seen in any patient. The one with fever and rash responded with complete disappearance of both within 48 hours, while the pain and tenderness over the bubo remained for another two days. This swelling disappeared completely at the end of 18 days. Patients were followed up for one to four months. No recurrence was seen in any of them but one patient came back six weeks after the trial with proctitis, for which no cause could be detected. No untoward side-reactions were observed during the trial.

Medical Women in the National Plan.—B. Mendonca (*Journal of the Association of Medical Women in India*, vol. 47, February, 1959) stated that antenatal and postnatal care, safe delivery, and proper guidance in the rearing of children cannot be properly handled unless there is a sufficient number of women in health-related fields. There are about 650 qualified dentists in India—only a fraction of the total requirement. As the pregnant woman and the toddler need both preventive and curative dental treatment, it has been decided to train women as dentists and dental technicians. There is also a marked shortage of nurses, health visitors, midwives, and other ancillary personnel. The presence of more women doctors in villages will help to reduce infant and maternal mortality. About 300 urban and 2,000 rural clinics for family planning will be set up where women doctors can render an important service. The woman doctor can also give proper guidance regarding the dietary needs of children and adults.

Vasectomy.—H. S. Lakhtakia (*Journal of the Indian Medical Association*, vol. 32, March 1, 1959) performed vasectomy for the purpose of sterilization on 100 men during a period of one year. Most men operated on were in the age group 41 to 50, but a few were between 21 and 30 years of age. Most of them belonged to the middle class and had up to six children. Only one with but two children submitted to the operation. No psychological disturbance was observed after the operation. Four developed fever, and wound infection occurred in seven in the postoperative period. P. S. Jhaver and co-workers reviewed another series of 682 vasectomies. In their series 14 men proved sensitive to local anesthetics; 3 complained of sexual debility after the operation, but this was relieved by psychotherapy. Hemorrhage and gangrene of the testis occurred in two; hematoma of the scrotum in seven; and scrotal abscess in three.

Planned Parenthood.—The sixth International Conference on Planned Parenthood was held in New Delhi in February. An appeal was made to the United Nations Human Rights Commission to include in the Declaration of Human Rights the right of voluntary parenthood and freedom to obtain family-planning education as a basic human need. The conference urged the food and agricultural organizations of its member nations to combine their efforts to increase food production with programs for planned parenthood. It appealed to the World Health Organization to include contraceptive information as an integral part of its health programs. The conference stated in its resolution that, while the WHO had rendered outstanding service in improving human health and reducing the death rate, it had made no corresponding effort to educate people in limiting the size of their families. It asked the Economic and Social Council of the United Nations to consider measures of planned parenthood as a major means of improving living standards.

Intestinal Amebiasis.—S. P. Mehta and co-workers (*Journal of the Indian Medical Association*, vol. 32, March 1, 1959) treated adults who had acute, subacute, and chronic amebiasis with 0.5-Gm. tablets of α-dichloroacetamido-β-chloro-p-chloropropiophenone (compound 1), 0.25-Gm. tablets of N-(β-oxyethyl)-N-[*p*-phenoxy (1′-nitro)-benzyl]-dichloroacetamide (compound 2), and 0.1-Gm. tablets of N-(β-ethoxyethyl)N-[*p*-phenoxy (4′ nitro)-benzyl]-dichloroacetamide (compound 3). The dosage of each was two tablets three times a day for 10 days. Proctoscopy was performed on all patients before treatment and rectal swabs were collected for study. After 10 days of therapy stools were examined daily for a week. The patient was considered cured if the stools remained free of ameba throughout the week. Compound 1 was given to 11 patients the duration of whose illness was one to five years. One had hepatic involvement. Eight were cured after treatment with this drug, a 72% rate of cure. Compound 2 was given to 22 patients the duration of whose illness was 1 to 10 years. Three had hepatic involvement. Seventeen were cured, a rate of about 77%. Compound 3 was given to six patients the duration of whose illness was one to three years. Only two received the full course of treatment, so the results were inconclusive; three patients who received the drug for a week were cured. No toxic effects were noticed in any of the patients undergoing the clinical trial with the three new compounds.

UNITED KINGDOM

Scotland's Health.—The annual report of the Department of Health for Scotland stated that the general trend of Scotland's health continued to be favorable, but, as in England and Wales, the rising incidence of lung cancer and coronary atherosclerosis caused alarm. The incidence of and mortality from chronic bronchitis were high. This was attributed to the climate and to the increasing industrialization of Scotland. Men over the age of 45 were the only group of the population with a rising death rate, due almost entirely to lung cancer, bronchitis, and heart disease. The infant mortality of 27.7 per 1,000 births was the lowest on record. In Glasgow, which is heavily industrialized, it was 35. It was suggested that one way of reducing this and of improving health generally would be to decentralize the population from the industrial urban areas. There were about 20,800 patients in mental hospitals, or about 1 in 240 of the population; 75% of these were compulsorily detained in the first case, 17,370 have been hospitalized for more than a year, 13,551 longer than 5 years, and 7,376 for more than 15 years.

Medical Aspects of Polar Exploration.—The medical and physiological aspects of the Fuchs-Hilary Commonwealth Trans-Antarctic expedition were discussed by Goldsmith, who accompanied the expedition as medical officer and physiologist (*Lancet* 1:741, 1959). The advance party of eight, whose work it was to prepare a base and make the scientific observations, lived in an unusually primitive fashion and were exposed to cold stress as severe as that ever experienced by man. They suffered from no serious illnesses, nor was there any sign that the rigorous life they endured left any permanent ill-effects. They were subjected to severe physical strain, as snow and ice had to be moved and temporary buildings erected under conditions of severe cold.

At first a temperature of —30 C and a wind of 20 knots was a signal to seek shelter, but they soon became acclimatized and were able to work in temperatures of —45 C. No difficulty was experienced in breathing, nor was there any evidence of pulmonary damage at these low temperatures. The men were able to work with their bare hands, handling heavy metal parts and servicing engines at —36 C, although even simple jobs took five or six times as long as in normal surroundings. For nine months the men lived in a crate 20 ft. long, 9 ft. high, and 7.5 ft. wide, the temperature of which rarely rose above 7 C. Ventilation was a problem, and there was evidence that the fumes from the paraffin heaters caused mild chronic carbon monoxide intoxication, manifested by headaches, nausea, vomiting, and conjunctivitis. If fresh air was let in the living conditions were too cold.

Food, which was canned or dehydrated, was described as nutritionally adequate but uninteresting. All took turns at cooking, an oil drum being improvised as an oven. Body weight fell or remained steady and body fat thickness measurements showed little change. Clothes consisted of layers of normal clothing with outer windproof coverings. There were no facilities for washing clothes. Cold hands and feet were due to unevaporated perspiration. As the men became acclimatized they wore less clothing. They slept fully clothed in tents, which were unheated except on going to bed and getting up.

Although much medical equipment was taken little of it was needed. Minor degrees of frostbite were never troublesome. Cuts, abrasions, and cracks of the fingerpads and hands took a long time to heal. For the first few months some of the men suffered from aching pains, stiffness, and swelling in the finger joints, which was worst in the morning and improved as the day went on. Infections of any kind were rare. Sore throat and loss of voice occurred in the early part of the winter, but this did not seem to be infectious as there was no malaise or pyrexia and was probably due to the drying effect of cold air. There were no cases of common cold. One case of acute peptic ulcer occurred. It was difficult to provide bed rest in a tent at —30 C for this man, and the nearest thing to a light diet available was canned herrings in tomato sauce. Because there were a number of cases of severe indigestion, antacids were the most frequently used medicaments. Accidents were rare and in the whole year only one man-day was lost from this cause. There was some evidence that dental fillings deteriorated in the cold and that dental caries continued as fast as if not faster than in temperate climates.

Neurogenic Arthropathy After Administration of Hydrocortisone.—The intra-articular injection of hydrocortisone acetate for the treatment of arthritis has been widely accepted for about eight years. Most reports stress the subjective benefit, including freedom from pain, and the few side-effects, which occur in only about 2% of patients. There has been no suggestion that repeated intra-articular injections of hydrocortisone could seriously aggravate the arthritis, yet this might be expected as a result of the relief from pain. Pain is a protective mechanism, and its relief might well encourage excessive weight-bearing and mobility, thereby accelerating destruction of the interior of the joint. Chandler and co-workers observed this in 10 of 18 patients with arthritic pain who had prolonged treatment by intra-articular injections of hydrocortisone (*Brit. M. J.* 1:952, 1959). In one patient with osteoarthritis a neurogenic arthropathy developed in a hip joint after he had weekly injections for a year, during which 900 mg. of hydrocortisone was administered. Examination after this time showed an extremely mobile painless joint, which on radiography showed gross destruction of the femoral head and the roof of the acetabulum. There was no evidence of neurological disease or syphilis as in the usual patient with neurogenic arthropathy. Rheumatoid arthritis, tuberculosis, and other infectious processes were excluded. The repeated injection of hydrocortisone into a joint is regarded as potentially dangerous. It should be done only under careful radiologic supervision.

Hypothermia for Cardiac Surgery.—Visual intracardiac surgery can be performed with the use of either hypothermia or a pump oxygenator. A combination of the two has been used experimentally. Hypothermia, by lowering the body's oxygen requirements, lessens the demand on the pump oxygenator during cardiopulmonary bypass; it is thus possible to simplify the machine and use less donor blood to prime the extracorporeal circulation, but it has been usual to limit cooling to about 29 C (84 F) because of the fear of irreversible ventricular fibrillation at lower temperatures. Drew and co-workers showed that it was possible with an extracorporeal blood circuit to cool dogs to 10 C (50 F) and to produce complete cardiac arrest for 30 minutes without damage (*Lancet* 1:745, 1959). They extended the technique for use in cardiac operations on human beings (*Lancet* 1:748, 1959). They used a simplified circuit, omitting an artificial oxygenator, with two blood pumps directing most of the systemic and pulmonary venous streams from the atria into reservoirs from which the blood was pumped into the aorta and pulmonary artery respectively.

The patient's own lungs were thus used for their normal function of oxygenation. The temperature of the patient was reduced to 15 C (59 F) by passing the blood through a heat exchanger surrounded by a mixture of methyl alcohol and solid carbon dioxide. When this was achieved the pump circulations were stopped so that the surgeon had about 45 minutes to operate on the empty heart without any serious risk. Most intracardiac procedures can be completed within this time. At the end of the operation the blood was rewarmed by water at 40 to 44 C (104 to 111 F) in the heat exchanger.

The advantages of this technique are that the blood itself acts as a refrigerant, no external cooling of the body being necessary; there is no hemolysis as there is with the heart-lung machine; there is no plasma-electrolyte disturbance; and there have been no postoperative lung complications. With the pump used only for cooling and rewarming and not during the operation the duration of the heart bypass is kept down to a reasonable period, and this reduces the risk of hemolysis. The author considered that there was no reason why cooling should not be carried below 15 C in man. He has cooled dogs to 8 C (46 F) and rewarmed them without harm. Three children with congenital intracardiac lesions were operated on by the new technique. The first died from heart block after partial correction of a persistent atrioventricular canal which was virtually inoperable. After total circulatory arrest for 46 minutes the child appeared to be recovering. The other two children survived. One had right atriotomy and ventriculotomy for obliteration of an atrial and ventricular septal defect, and the other had a repair of a ventricular septal defect. Ventricular fibrillation did not occur, and there were no significant biochemical upsets and no evidence of neurological or other damage.

CORRESPONDENCE

OPEN-HEART SURGERY

To the Editor:—I was disturbed by some statements made by Henderson and associates in The Journal, May 2, pages 28-32, relating to the need for physiological monitors during open-heart surgery. When one undertakes surgical bypass of the heart and lungs for open-heart operations, thus eliminating the vitally normal functions of the heart and lungs, good sense dictates that we know how effectively we have substituted the man-made for the God-made machinery. Without such knowledge anything we do to maintain a *status quo* as close to normal as possible becomes purely empirical. In such situations mistakes can be made over and over again without our knowing why.

For example, there is the simple matter of how well the blood is being oxygenated. How does one know this unless it is being measured? Studies indicate that even with experienced observers cyanosis cannot be reliably detected until the oxygen saturation has fallen to 80% of normal. Is it possible that oxygen lack is of no consequence, or can we assume that if the oxygenator functions at a certain speed everything is all right? Anyone who has operated a pump oxygenator knows that this is not so. There is no substitute for making accurate measurements. The same might be said for cardiac rhythm, carbon dioxide blood levels, arterial pressure, various other pressures, body temperature, the temperature of the oxygenator, and brain wave activity. There is no reason for ignoring these physiological parameters.

I agree with Dr. Henderson that simplicity should be the governing rule and that the prime interest of the team is the swiftest and safest route, but simplicity cannot be unerringly equated with safety. We must make those measurements that are necessary to assure safety. A few years ago at one well-known clinic about a dozen physiological variables were being monitored during open-heart surgery. Today, this number has been reduced because experience with an extremely complicated electronically controlled pump oxygenator has shown its reliability. In the average patient on whom the pump oxygenator is used today, no such control is available, and to do an intelligent job we have to measure several physiological variables.

I cannot agree, therefore, with Dr. Henderson. It would be dangerously misleading to tell people who may be unfamiliar with the heart-lung bypass that monitoring appliances serve to confuse uninitiated minds. Rather we might advocate that the uninitiated learn to use these monitoring devices intelligently for a better understanding of what is taking place during the procedure.

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HAZARDS OF PLASTIC BAGS

To the Editor:—In The Journal, April 25, page 2021, there is a note concerning the hazards of discarded plastic garment bags. I suggest that the plastic bag manufacturers be required to print in large letters a statement about the hazards of the bags and a request for their safe disposal.

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Note: A follow-up of the item referred to appears in this issue under Medicine at Work.—Ed.

IODINE IN NAIL POLISHES

To the Editor:—It has come to my attention that certain nail polishes contain inorganic iodine or compounds containing iodides. Those physicians who use radioactive iodine studies in thyroid evaluation should be alerted for this possible contaminant. Several patients seen recently apparently absorbed enough iodine to elevate the protein-bound iodine level as well as depress the thyroid uptake. Recognition of this in tabulating the results of laboratory studies is important. I am not aware that this information is generally appreciated by members of the medical profession.

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CARDS SUGGESTED ON DISCHARGE FROM HOSPITAL

To the Editor:—Physicians frequently treat patients who come from various parts of the country. Many of these patients have previously undergone operations and often they will be indefinite as to the kind and date of the operation, the name of the surgeon, or the location of the hospital where the operation was performed. Yet many times it is most important to know as soon as possible the nature of the previous operation. For instance, the patient may state that she had an operation on "a tube and ovary" or for a "false pregnancy." The physician may want to know which ovary was operated on, whether it was resected or fully removed, and whether an appendectomy was performed at the time. The answers to such questions and others may be important guides toward a correct diagnosis.

Under present circumstances it is often impossible to get that information, and even if the patient should know the date and place of the operation it might take weeks before such information could be obtained from a hospital in a distant city. To obviate this difficulty I would suggest that hospitals be requested to furnish each patient on discharge with a card stating the nature and date of the operation performed. In these days of cards, one more should not prove too burdensome to the average person, especially when such a card may be of great help in some future medical emergency.

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DISAPPEARANCE OF METASTASES

To the Editor:—The paper by Kessel in The Journal (169:1737-1739 [April 11] 1959) on spontaneous disappearance of pulmonary metastases from a clear-cell renal carcinoma was of great interest, but I was troubled to note that the presumed metastases had not been so proved by thoracotomy, biopsy, and microscopic examination. The x-ray appearance was admittedly suggestive of this type of tumor, but without ultimate proof, one cannot accept this report. This is doubly regrettable because of its great interest and importance. If Dr. Kessel has additional information on this point, he should let us know.

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To the Editor:—The appearance of the lesions in the roentgenograms was so characteristic for pulmonary metastases (rounded and sharply limited, almost homogeneous, large in size and few in number, and growing rapidly in a patient who lost much weight in a short time) that they were read as metastatic in nature even before the primary tumor was found. When a nephrectomy was performed and an adenocarcinoma was found, the diagnosis of metastases became definite. Many statements appear in the literature about the value of roentgenograms in the diagnosis of pulmonary metastases. Rigler, in "Outline of Roentgen Diagnosis" (Philadelphia, J. B. Lippincott Company, 1954, p. 93), wrote that in almost all cases the diagnosis of pulmonary metastases can be definitely made by this means alone, as the lesions, even in their early stages, are very characteristic. In "The Chest and the Heart" (edited by Myers and McKinlay, Springfield, Ill., Charles C Thomas, Publisher, 1948, vol. 1, p. 370), it is stated that the presence of multiple spheric tumors in one or both lungs, seen in the x-ray film, almost always means neoplastic metastases. Hinshaw and Garland, in "Diseases of the Chest" (Philadelphia, W. B. Saunders Company, 1956, p. 351), stated that pulmonary metastases should rarely be diagnosed with finality from roentgenograms of the chest unless a primary malignant tumor is known to exist.

In the case presented in my paper the characteristic roentgenograms and the primary tumor, an adenocarcinoma with metastases to the abdominal lymph nodes, were present. The disappearance of the metastases after nephrectomy without any treatment would be an additional proof that the existence of these lesions was connected with the presence of the adenocarcinoma. Even if we would like to accept in this case the possibility of any pulmonary disease other than metastatic, it would be almost impossible to find a disease which could produce symptoms and findings as in the presented case.

The disappearance of the metastases as shown in the roentgenograms of the chest was also not proved by thoracotomy, biopsy, and microscopic examination. It is understandable that nobody would perform such an operation on a healthy person only to prove that something does not exist, but even if it were done, a negative result would not prove anything. The complete recovery of my patient and the fact that the chest x-rays remained clear for many months after nephrectomy would make it highly probable that the metastases disappeared completely.

In such cases the problems of how frequently the pulmonary metastases disappear after nephrectomy, whether they disappear completely or only regress to the point where they become invisible in the roentgenogram, whether metastases to organs other than the lungs also disappear after the nephrectomy, and whether specific antibodies can be found in patients in whom the metastases disappeared spontaneously are still unsolved. These problems need further investigation, as until now few such cases have been reported.

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MEDICAL LITERATURE ABSTRACTS

INTERNAL MEDICINE

Electrocardiographically Recorded Changes in Cardiac Activity During Catheterization of the Right Heart and the Pulmonary Artery. M. V. Muraviev, P. M. Zlochevsky and G. V. Gromova. Terapev. Arkh. 31:22-29 (no. 2) 1959 (In Russian) [Moscow].

The authors studied electrocardiographic changes in 50 patients with diseases of the heart and lungs during catheterization of the right heart and the pulmonary artery. They noted transitory disorders of the rhythm and conductivity in 56% of the cases. These consisted of single or group extrasystoles, paroxysmal tachycardia, atrioventricular dissociation, etc. The rhythm changes were intimately related to the mechanical irritation of the endocardium by the catheter tip and much less so to the degree of the heart disease. They were transitory in character and disappeared as the catheter was moved or withdrawn. Good tolerance of cardiac catheterization proves its relative safety and gives no grounds to consider such disorders of the rhythm and conductivity as complications.

The Significance of Serum Transaminases in the Detection and Prognosis of Myocardial Infarction. K. Bobek, V. Carlicek and V. Lan. Terapev. Arkh. 31:54-60 (no. 2) 1959 (In Russian) [Moscow].

The activity of glutamic oxalacetic transaminase (GO-T) was investigated in 100 patients suspected of having a fresh myocardial infarction. In 41 patients the diagnosis of infarction had been made electrocardiographically; in 13 it had been made clinically with the aid of the usual laboratory tests; in 26 there was stenocardia without definite diagnosis of infarction; in 20 pains were caused not by the disease of the myocardium but by some other illness (embolism of the pulmonary artery, bronchopneumonia, rheumatic carditis, necrosis of the pancreas, etc.). In 54 patients with fresh myocardial infarction, 51 had their GO-T activity tested in appropriate time limits, and it was considerably increased (205 units on the average) in all. Patients with stenocardia had normal enzyme levels. Increased GO-T level was seen not only in patients with myocardial infarction but also in those with pulmonary infarction, rheumatic carditis, and acute pancreatic necrosis. In 9 patients with myocardial infarction whose GO-T activity exceeded 300 units, there were 3 deaths, and 4 cases ran a severe course. In 27 patients whose enzyme level varied between 100 and 300 units, the disease ran a milder course, and there was only one death. Of 15 patients whose GO-T activity was below 100 units, none died, and all had a very light form of the disease.

Rickettsioses and Cardiovascular Affections: On the Basis of 27 Cases. P. Michon, P. Giroud, L. Mathieu and others. Bull. et mém. Soc. méd. hôp. Paris 75:23-32 (no. 1-2) 1959 (In French) [Paris].

A systematic search for rickettsioses by the microagglutination technique in patients with cardiac diseases of almost all kinds, arterial, arteriolar, or venous, the origin of which was not immediately evident, revealed a surprisingly large number of positive serologic findings. The patients studied were drawn from 2 services of general medicine and 1 of cardiology. They consisted essentially of men, although the statistics are somewhat misleading in this respect because one of the services was military. Almost all the patients were young, with no signs of atheroma. A history of residence in regions in which typhus is traditionally endemic was often given, but some of the subjects had never been out of France. Several factors (tobacco, frostbite, fatigue, privation) often seemed to be intermingled. The causative Rickettsia organisms were of various types, with a slight preponderance of the epidemic and murine forms. Several varieties sometimes seemed to be involved in the same person (even after elimination of the coagglutinations). The agglutination levels were highly variable; in general, the most elevated levels were seen in the youngest subjects. The agglutination level is probably the higher the closer the rickettsial primo-infection (or primo-infestation). Treatment with antibiotics, except in 2 cases, was generally of little effect.

The frequency with which positive findings were obtained in these patients suggests that the possibility of rickettsioses should always be considered in the diagnosis of an apparently primary cardiovascular process. Several facts support this opinion. These are (1) the historic parallelism between Brill's disease and Buerger's disease, the geographical distribution of thromboangiitis and zones of endemic

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typhus (the significance of which is denied by some authors), and the frequency of arteritis and primary endocarditis after the world wars and its connection with typhus; (2) the well-known occurrence of early cardiovascular complications in the course of rickettsial diseases; and (3) late vascular complications. Biological reactions that reveal, directly or indirectly, the responsibility of the Rickettsia organisms in cardiovascular disease can often be obtained in the absence of evocative clinical findings. The angiotropic character of both the major and the minor rickettsioses must be emphasized. Fraenkel's nodule, the basic lesion of historic typhus, is formed by a thrombosing endovascularitis with perivascularitis, affecting chiefly the arterioles but also the arteries, and swarming with Rickettsia organisms. Modern data on the rickettsial cycle and immunity serve to explain the fact that the vascular processes attributable to Rickettsia organisms often appear long after the primary infection. The resurgence is analogous to that found in Brill's disease; the association of various factors and the reaction of the terrain account for the general and vascular reactions responsible for the many clinical forms assumed by cardiovascular disease of rickettsial origin.

Cycloserine in Cases of Recent Exudative Tuberculosis Not Previously Treated with Chemoantibiotics. B. Mariani. Riv. pat. e clin. tuberc. 31:549-571 (Nov.-Dec.) 1958 (In Italian) [Bologna, Italy].

The author reports on the effect of cycloserine in 4 patients, 2 men and 2 women, ranging in age from 25 to 63 years, with recent exudative tuberculosis. The patients had not been treated previously with chemoantibiotics except the 4th one who had received small doses of streptomycin and isoniazid but had not benefited from either of them. The general condition of the latter patient improved (although only temporarily) as soon as treatment with cycloserine was begun; the body weight increased, the lesions regressed, and Koch's test became negative. In the remaining 3 patients cycloserine therapy brought about a rapid and marked improvement in the general condition; cough regressed and disappeared, temperature dropped, and expectoration diminished and eventually ceased; Koch's test became negative within 2 months, and other laboratory tests gave normal results in a short period of time. Two of the patients recovered, and the third improved so markedly that he was well on the way to recovery.

The administration of cycloserine had no serious side-effects. With the exception of a temporary dizziness which was observed at the beginning of the treatment, the only side-effect was an attack of epilepsy, which occurred once in the 3rd patient. The effect of cycloserine on the objective symptoms was similar to that obtained with the combined treatment with isoniazid and streptomycin. The regression of the roentgenologic signs was marked, fast, and total in the first 2 patients, slow but marked in the 3rd, and poor in the 4th. The author believes that cycloserine, which up to this time has been used widely in the treatment of chronic tuberculosis, is also useful in the treatment of recent exudative tuberculosis. This is especially true if cycloserine is combined with other drugs, such as isoniazid, which would help to stabilize its good effect and avoid relapses.

Pleural Effusions of Viral Origin: On the Basis of 45 Cases. P. Michon, J. Nivière, A. Lercan and others. Bull. et mém. Soc. méd. hôp. Paris 75:33-42 (no. 1-2) 1959 (In French) [Paris].

Pleural effusions of viral origin may be divided into 2 groups—those accompanying pulmonary disease due to a virus infection, and those that may be called autonomous because they appear alone and are not attributable to any of the standard causes. The term "autonomous" is not strictly accurate, because it cannnot be definitely stated that there is no discrete underlying involvement of the parenchyma. Study of 175 patients with acute pulmonary disease seen at the hôpital militaire Sédillot during the winters of 1956-1957 and 1957-1958 showed that 35 (20%) had pleural involvement accompanying pulmonary disease of viral origin. Most of these pleural reactions were attributable to serologically confirmed influenza; those in which proof of origin was not obtained occurred in patients belonging to the same units, so that there were every reason to believe that the pleurisy was influenzal (virus A, Asiatic strain). Clinically, the effusions may appear early (the commonest type) or late (only 2 cases in this series). They may be caused by any of the known viruses responsible for acute pulmonary disease. The viruses of influenza are naturally those found most often, but patients with ornithosis-psittacosis and rickettsiosis may exhibit pleural involvement and cases due to the adenopharyngoconjunctival (APC) viruses have also been observed.

Autonomous pleural effusions for which a viral origin has either been proved or is suspected are infrequent. The clinical picture is often atypical. The onset is generally insidious but may at times be abrupt. At the height of the disease, the general signs are dominated by a temperature of 38 to 38.5 C (100.4 to 101.4 F) and by asthenia, often marked. The functional symptoms consist of an intense stitch in the side and cough which, unlike the dry cough usually found in pleurisy, is often productive. Radiography confirms the existence of the effusion, but biological studies are needed to establish its viral origin. Autonomous pleurisy may be accompanied by viral pericarditis or a variety of other manifestations of viral infection, e. g., the hematuric nephritis sometimes seen in patients with influenza.

Pleurisy due to viral infection must be distinguished from that caused by tuberculosis, neoplasms, allergic disorders, heart disease, or other less common conditions. Therapy includes the administration of anti-inflammatory drugs and especially antibiotics. Oxytetracycline given to the authors' patients in a dose of 1 Gm. daily produced a rapid improvement in the general signs and functional symptoms. The prognosis is always good; the effusions often disapear rapidly, and rediologic resolution is usually complete.

The Natural History of Carcinoma of the Lung. G. L. Emerson, M. S. Emerson and C. E. Sherwood. J. Thoracic Surg. 37:291-304 (March) 1959 [St. Louis].

In recent years diagnostic methods, such as bronchoscopy, cytology, biopsy studies of the scalene node, and thoracotomy, have proved helpful in diagnosing carcinoma of the lung earlier. However, since a significant change on the chest roentgenogram often precedes clinical symptoms, it was the aim of this study to gain new information about these early changes and to observe the alteration in such x-ray shadows with the passage of time. To this end the cases of more than 400 patients with pulmonary cancer seen at the Strong Memorial-Rochester Municipal hospitals, Rochester, N. Y., were reviewed. This report covers 360 proved cases, the majority having been diagnosed within the past 15 years. Records were abstracted and information was solicited from surviving patients, families, physicians, hospitals, and other institutions where roentgenograms may have been taken. Any past roentgenograms available were gathered and reviewed in conjunction with later films made at the time of diagnosis of the patient's carcinoma. A table presents a clinical analysis of 10 of the 360 patients (2.8%) who survived 5 years or more. Other tables record the average interval elapsing between the earliest roentgenographic evidence of the individual's cancer and the clinical or pathological diagnosis. In reviewing earlier films, changes have been sought which could be correlated with the eventual, grosser evidence of the neoplasm. The types of change seen and their frequency are recorded in another table.

The authors emphasize that an average interval of almost 7 months between the first symptom and the clinical diagnosis emphasizes the need for improvement in cancer education of the public and the medical profession. Again, an interval between the observation of abnormal x-ray shadows and diagnosis of 4 months for all cases, or almost 16 months for a smaller group, plays a prominent part in the delayed diagnosis of pulmonary cancer. Hilar, mediastinal, and large parenchymal masses, as well as gross atelectasis, produce roentgenographic shadows strongly suggesting carcinoma and are of serious prognostic import. Somewhat less obviously produced by a cancer but to be viewed with a high degree of suspicion are obstructive pneumonitis, the small hilar nodule, localized emphysema, and thick-walled irregular abscesses. These carry a slightly less grave outlook, when diagnosed without delay. The isolated parenchymal nodule should be regarded as malignant until proved otherwise. The smaller the nodule, the less apt it is to have other associated roentgenographic changes, and the better is the prognosis. It is felt that the small persistent infiltrative density should be viewed with almost as much suspicion as the isolated nodule. It will most frequently be confused with a residual fibrous change from inflammatory disease, and the distinction, on pure roentgenographic grounds, is often impossible with a single film. As in the study of changes in the hilar region, the review of current films with any other previous films is of great aid in evaluating the parenchymal nodule and infiltrative density.

The abnormal film which is read as normal is another factor in late diagnosis of carcinoma of the lung. This can happen to even the most experienced, and the authors feel that double reading of films, particularly of normal films, would reduce this factor. About 44% of the patients in this series had no film taken prior to the time of diagnosis, or none was available. Yet, the changes present on admission films were such that many patients would have had positive roentgenograms if films had been taken during the preceding year. The general increase in mass surveys among persons over 40 years of age must be supported, and patients must be encouraged to obtain periodic x-ray studies of the chest along with physical examinations. The individual should be encouraged to have routine x-ray studies done at the same roentgenologic unit for better comparison follow-up.

Investigations in Hepatolenticular Degeneration. M. Plooij, J. van der Meer and A. Kaag. Nederl. tijdschr. geneesk. 103:200-204 (Jan. 31) 1959 (In Dutch) [Amsterdam].

The authors describe observations on 2 siblings with hepatolenticular degeneration (Wilson's disease). One of the 2, a girl, had been well until the age of 14 years, when speech became difficult and she complained of headaches. At age 17, hepatolenticular degeneration was diagnosed on the basis of a neurological examination, which revealed a constant grin, open mouth, coarse head tremors, intention tremors of the hands, monotone slow speech, Kayser-Fleischer ring of the cornea, poor psychological contact, and hepatic disturbances. The brother of this girl, who was 2 years older, was observed at a military hospital, where examination revealed enlargement of liver and spleen. When it was learned that the sister had hepatolenticular degeneration, a Kayser-Fleischer ring was discovered in the brother, along with abnormalities in the urinary excretion of copper and of amino acids. On the basis of these and other symptoms, the youth's disorders were likewise recognized as manifestations of hepatolenticular degeneration.

Further studies were made on the function of the liver and on the copper and amino acid metabolisms, and particular attention was given to the effects achieved with various therapeutic measures. The effect of various drugs on the copper metabolism, such as dimercaprol, calcium edathamil (Ca-EDTA), and particularly penicillamine, was determined by means of balance tests. When penicillamine was administered by mouth in daily doses of 600 or 900 mg., it greatly increased the urinary elimination of copper, and there was a noticeable reduction in tremor. The favorable effect of penicillamine on the elimination of copper was thus confirmed, and it is suggested that the early administration of penicillamine may inhibit the development and progression of cerebral defects. It has not been determined whether it will be possible to exert a favorable influence on the hepatic cirrhosis and on the amino acid metabolism.

Intestinal Parasitism in a Rural Patient Population. J. J. Kirschenfeld. GP 19:93-97 (March) 1959 [Kansas City, Mo.].

Intestinal parasitism is still prevalent in rural areas in some parts of the South. In an attempt to determine its incidence in 228 patients who were seen routinely in an office practice in Alabama, the patients were supplied with 3 containers, each consisting of 2 small glass jars; one jar contained 5% formalin, the other polyvinyl alcohol fixative. Two series of fecal specimens were collected, the patient being advised to add a marble-sized piece of feces to each preservative and to emulsify thoroughly with the applicator sticks provided. A third specimen was collected after a purge with sodium chloride solution, about 10 cc. of the feces being added to each jar. These specimens were then mailed to the State Health Department Laboratory for examination. The polyvinyl alcohol fixative contents were smeared on slides, then stained by a modified hematoxylin method. The formalinized feces were filtered through coarse gauze; ether was then added, and the tube centrifuged (Ritchie method). The Willis salt flotation method was also applied on some of the formalinized fecal specimens. The combination of these methods makes possible a complete, effective parasitological examination on specimens transmitted over long distances through the mail, regardless of temperature conditions or delay.

Eighty (35%) of the 228 patients harbored parasites; the infestation rate was slightly higher in white patients than in Negroes, with only slight differences by sex. Of the 80 patients with positive feces, 40 (50%) harbored a single parasite, 21 harbored 2, 9 harbored 3, and 10 had 4 or more parasites in their feces. It is significant that 60% of the patients infested with multiple parasites were also infested with Endamoeba histolytica, which was found in 26 patients (11.4%). E. nana was present most often and was found in 35 patients (15.3%). Hookworm ova were found in 9.2% of the stools. Forty per cent of the symptomatic patients and 28% of the asymptomatic patients had positive feces. There was no correlation between the individual symptoms and the presence of parasites. The combination of diarrhea, abdominal discomfort, and anorexia produced the highest yield in positive feces. These findings showed that detection of intestinal parasitism can be made a part of routine office practice.

Nephrotic Syndrome with Bilateral Thrombosis of Renal Veins in Two Patients with Cardiac Disease. J. T. Balsløv. Ugesk. læger 121:197-200 (Feb. 5) 1959 (In Danish) [Copenhagen].

In bilateral thrombosis of the renal veins, development may often be insidious and present the picture of a nephrotic syndrome with varying degrees of renal insufficiency. A nephrotic syndrome developed in 2 elderly adipose patients with decompensated heart disease, who had been treated with mercurial diuretics. Autopsy revealed bilateral thrombosis of the renal veins. The treatment with mercurial diuretics is thought to have been important in the development of the thrombosis. In a number of cases of this disorder, examination reveals enlarged kidneys. Sometimes intravenous urography shows a picture as in cystic kidney. The diagnosis of bilateral thrombosis of the renal veins depends mainly on the exclusion of other causes of a nephrotic syndrome: heart constriction, intoxication with heavy metals, diabetic nephropathy, amyloidosis, lupus erythematosus disseminatus, and glomerulonephritis in nephrotic stage. Renal biopsy will be helpful. Therapy is first and foremost anticoagulation treatment, together with antibiotic treatment of complicating infections. The prognosis is unfavorable. Few patients with the disease have lived more than a few months after the symptoms set in. Death is due to renal insufficiency, infections, or other thromboembolic complications.

Arterial Pressure in Healthy Older People. W. F. Anderson and N. R. Cowan. Clin. Sc. 18:103-117 (Feb.) 1959 [London].

The authors studied the arterial pressure of 306 men and 240 women who ranged in age from 60 to 89 years. They were selected from 517 men and 503 women on the basis of a complete clinical study which included ophthalmoscopic and rectal examinations with urinary analysis. A routine chest x-ray was taken, which for those over 70 years included left lateral films of the chest, cervical spine, and skull. Weight and height were ascertained, and on the basis of a social history the persons selected were considered to be well adjusted and contented in their environment.

The means, standard deviations, and coefficients of variation are presented for 5-year age groups. The regression of systolic blood pressure on age is represented by a simple parabolic function, and that of diastolic blood pressure on age by a straight line. Systolic and diastolic blood pressure means increase with age, and the increase is greater for the systolic. Women show higher mean values than men at all ages, but the differences between the means for corresponding ages are not significant in these data. The range of blood pressure in healthy older persons is wide, and systolic blood pressure readings in the highest age range (80-89 years) reach a figure of 220 mm. Hg for men and 230 mm. for women. Irrespective of age, diastolic blood pressures of up to 104 mm. Hg for men and 108 mm. for women are found. As people age, the average values for blood pressure increase, and this is particularly so for the systolic pressure. The blood pressure means of women are consistently higher than those of men.

On the Frequency, Prognosis and the Early Diagnosis of Periarteritis Nodosa. V. E. Liubomudrov. Terapev. Arkh. 31:50-54 (no. 2) 1959 (In Russian) [Moscow].

Periarteritis nodosa, as shown by the analysis of 1,009 case histories from the medical literature and of 10 personal observations, still remains an imperfectly known condition. In particular, its formes frustes have entirely escaped close study and have led to the generally accepted opinion in the literature that the disease is accompanied by a considerable mortality rate. On the contrary, analysis of a large number of case histories shows that periarteritis nodosa, correctly diagnosed during life, ends in recovery in the majority of cases. The initial and the favorably running forms of the condition have practically entirely escaped investigation. The author cites cases of early (including the ambulatory) diagnosis of periarteritis nodosa. One ought always to think of this disease when a patient presents general symptoms, along with the symptoms indicating lesions of a number of organs and systems.

Lipid Nephrosis: Lines of Guidance for Steroid Treatment Based on Case with 6 Recurrences: Variations in Serum Complement and 17-Ketosteroid Excretion. P. Hempel-Jørgensen. Ugesk. læger 121:192-197 (Feb. 5) 1959 (In Danish) [Copenhagen].

In a case of lipid nephrosis in a boy, aged 7 years, there were 6 recurrences in less than 2 years. Corresponding to the 7 proteinuria periods, 7 series of treatment were applied, with 60 mg. of prednisone daily for the first 10 days, then with gradually reduced dosage. In most cases the treatment lasted about 40 days. Every time during the prednisone treatment full remission set in around the 10th day of treatment, with complete cessation of proteinuria, increase in diuresis, loss of weight, disappearance of possible edemas, and reduction in sedimentation rate and serum cholesterol level together with increased serum protein. The serum complement, followed during one proteinuria period, showed subnormal values during the edema period, with rise to values above normal after remission, presumably as the expression of the presence of an antigen-antibody reaction in the edematous phase and with rise after remission as a rebound phenomenon. The 17-ketosteroid excretion in the urine, which was followed regularly for a year during 3 recurrences, showed characteristic increases in connection with these recurrences. The changes in the 17-ketosteroid excretion cannot be explained.

SURGERY

Vertebral Traction in Cervico-Occipitalgia. J. Levernieux and J. Fossier. Semaine hôp. Paris 35:559-564 (Feb. 18) 1959 (In French) [Paris].

Cervico-occipital algia is pain, usually chronic, situated at the level of the neck. This pain, which may be either unilateral or bilateral, may radiate to a distance, toward the scapular, thoracic, or anterior cephalic regions, and is often accompanied by multiple sensory disturbances. Traction on a mechanical table was used in treating 200 patients, most of whom were referred to the authors because they presented a cervical disk arthrosis. The mechanism of the table was so devised that the cervical segment could be treated electively between an occipitomental and a scapular point of attachment. The speed of traction and the separation of the tractor-trolleys could also be controlled by the operator. Radiologic checks made before and after traction showed that, when the trolleys had a spread of 4 cm., the muscles and ligaments were stretched. A separation of 7 cm. between the trolleys, on the other hand, resulted in enlargement of the intervertebral space by 1.5 mm.

Three clinical types of the disorder were distinguished on the basis of the clinical and radiologic findings: (1) cervico-occipital pain with or without radiation to the shoulder; (2) cervico-occipital pain with radiation to the front of the head; and (3) cervical pain with sensory disturbances. Traction acting solely on the muscles and ligaments relieved 56% of the patients with pain of the first type. Traction resulting in an enlargement of the intervertebral space was effective in 60% of the cases in which pain of types 2 and 3 was present. These therapeutic results, if they can be validly used in formulating an etiological theory, suggest that type 1 pain which is not radicular or traumatic in origin is due to a musculotendinous inflammation, and that pain of the other 2 types is the result of irritation of the sympathetic fibers in the narrowed intervertebral foramens.

Electrocardiography in the Surgery of Mitral Disease. Y. I. Rudiakov. Terapev. Arkh. 31:11-22 (no. 2) 1959 (In Russian) [Moscow].

Electrocardiographic syndrome of hypertrophy of the right ventricle is a reliable diagnostic sign and can serve as an indirect indication of an increased resistance in the pulmonary circulation. The dependence of the latter on the degree of stenosis of the left venous orifice is probably maintained even in cases of long standing. The author's observations show an almost complete concordance between the electrocardiographic syndrome of dextroventricular hypertrophy and the degree of deformation of the mitral valve as revealed at the time of operation or at autopsy. Thus, the much debatable conception of the autonomous character of the resistance in the pulmonary circulation and its irreversibility becomes in a number of cases the source of unjustified pessimism. The syndrome of "overexertion" of the myocardium of the right ventricle, revealed in the inversion of the T wave in the first chest leads, and the M-shaped QRS complex in lead V_1 were met with in single instances with pronounced mitral stenosis, i. e., much less frequently than in cor pulmonale. Changes in the electrocardiogram during the postoperative period are all very much alike and are characterized by the negative T wave in some or all the leads. Recordable usually from the 10th postoperative day, these changes last sometimes more than a month and reflect the third electrocardiographic stage of pericarditis caused by the traumatic lesions of the pericardium during the operation.

General Considerations Regarding Acute Reflex Cardiac Arrest. C. Hahn and F. Risch. Helvet. chir. acta 25:484-489 (Dec.) 1958 (In French) [Basel, Switzerland].

Acute reflex cardiac arrest may pose a legal problem for the surgeon, for he may be called to account if resuscitation was neglected. Whereas formerly it was accepted as a fatality against which nothing could be done, at present it is regarded as a state which must be diagnosed and treated. In case of cardiac arrest during an operation, it is essential to intervene as rapidly as possible. Ascertaining the blood pressure and electrocardiography are dispensed with. In case of disappearance of the carotid pulse, the following measures are taken immediately: (1) giving pure oxygen at first by means of mask and balloon and then by intubation and (2) opening the thorax in the 4th intercostal space, and the pericardium. Then there are 2 possibilities: 1. If there is no ventricular fibrillation, forceful bimanual massage may be sufficient or may be combined with intracardial injection of 10 cc. of 10% calcium gluconate; massage is continued until the carotid pulse is again perceptible. 2. If ventricular fibrillation exists, the defibrillator should be used; one should be available in every surgical department; the best results are obtained with a voltage of 200, with 2.5 to 3.5 amp., and with a shock stimulus lasting at the most 0.1 second. It is useless to defibrillate a heart with deficient oxygenation and of inadequate tonicity. If myocardial tonicity remains insufficient despite cardiac massage, it is advisable to resort to the injection of 1 mg. of epinephrine in 10 cc. of isotonic sodium chloride solution into the left ventricle, or to give an intravenous infusion of 40% dextrose.

RADIOLOGY

A Comparative Radiological Study of Reiter's Disease, Rheumatoid Arthritis and Ankylosing Spondylitis. R. M. Mason, R. S. Marray, J. K. Oates and A. C. Young. J. Bone & Joint Surg. 41B:137-148 (Feb.) 1959 [London].

Previous reports on the roentgenologic aspects of Reiter's disease (urethritis, conjunctivitis, arthritis) have mentioned periostitis, especially of the calcaneus, osteoporosis, "nonspecific" changes, or a high incidence of sacroiliitis. This report is concerned with roentgenologic studies on 3 groups of patients, all of whom were subjected to routine roentgenography of hands, feet, ankles (including the calcaneus), and pelvis. The roentgenograms of 144 patients were available for comparison; of these patients 25 had Reiter's disease, 81 had rheumatoid arthritis, and 38 had ankylosing spondylitis. With regard to sacroiliitis, the authors found that, when changes in the sacroiliac joints were mild, they were unable to distinguish any qualitative difference between the 3 diseases, but severe erosions, marked sclerosis, and particularly ankylosis were found only in Reiter's disease and in ankylosing spondylitis. There were significant differences in the time of development of sacroiliitis in that the incidence of this condition increased to 54% in the patients with Reiter's disease with a history of 5 years or more, but in the patients with rheumatoid arthritis with a similar history the incidence increased to only 15%.

It was found that florid periostitis is suggestive of Reiter's disease, and when it occurs on the plantar aspect of the calcaneus, it is probably pathognomonic. Simple spurring and erosion of this bone, however, were present in all 3 diseases. There were certain differences in the roentgenologic appearances of the hands and feet, but, except for the aforementioned periostitis, a roentgenologic distinction would be difficult on the basis of these changes alone.

The Changing Roentgenologic Picture in Pulmonary Tuberculosis Under Modern Chemotherapy. R. M. Friedenberg, N. Isaacs and M. Elkin. Am. J. Roentgenol. 81:196-206 (Feb.) 1959 [Springfield, Ill.].

The authors report the cases of 9 patients with pulmonary tuberculosis, which were selected to illustrate the rapid resolution that may be noted roentgenographically within a short time after specific antituberculotic chemotherapy. The selected types of pulmonary tuberculosis were grouped according to the predominant roentgen-ray characteristics as follows: 1. Exudative productive lesions, varying from the feathery, irregular, dense, somewhat hazily outlined lesions of exudative disease to the dense, sharply defined, discrete shadows more typical of productive lesions. Three of the 9 patients had exudative lesions of the productive type. 2. Cavitary lesions, often rounded, ragged, with complete loss of lung margins and areas of increased density around the margin. Two patients had this type of lesions. 3. Miliary lesions. One patient with hematogenous miliary tuberculosis has been presented. 4. Effusion, with the predominant feature of being a serous effusion, usually pleural, occasionally pericardial. The patient reported on had both pleural and pericardial effusion. 5. The last 2 patients had tuberculous pneumonia, resembling lobar or bronchial pneumonia but more widely distributed and less well demarcated as to lobes and lobules.

The roentgenologic findings in these 9 patients showed that productive, exudative, miliary, pneumonic, and cavitary forms of pulmonary tuberculosis responded dramatically to chemotherapy with isoniazid, streptomycin, and aminosalicylic acid, if marked fibrosis and caseation had not occurred. Reports by other workers revealed that many longstanding cases of chronic disease without extensive fibrosis showed rapid and marked improvement in patients who received proper therapy. The extent of involvement does not affect the prognosis of the disease today as it did before the advent of modern antimicrobial therapy. The presence, however, of abnormal anatomic changes of extensive fibrosis or caseation must still be regarded as a poor prognostic sign.

PHYSIOLOGY

Lavage of the Lung. J. A. Kylstra. Acta physiol. et pharmacol. neerl. 7:163-221 (no. 2) 1958 (In English) [Amsterdam].

The absence of adequate kidney function results in a rise in concentration of products of cellular metabolism in the extracellular fluid. Many investigators have searched for possibilities in removing noxious substances from the body by other means than excretion via the patient's own kidneys. Five main groups of procedures may be distinguished: one making use of donor kidneys; one employing hemodialysis; one making use of ion exchange resins; one in which extracellular fluid is removed in bulk; and, finally, one using natural exchange surfaces of the body. The author discusses these different methods and is concerned particularly with the methods employing natural exchange surfaces of the body, so-called corporeal dialysis. After citing previous reports on intestinal lavage, peritoneal lavage, and the use of the urinary bladder as a "dialytic membrane," he calls attention to the possibility of using a patient's own lung as a hemodialyzer.

Lavage of the lung would imply the filling of the alveoli with fluid. Many alveoli are completely filled with fluid in lobar pneumonia, but, after resolution of the pneumonic exudate, the fluid is absorbed, and there usually remains no damage to the lung. One single lung, provided that it is not diseased, will suffice for the gaseous exchanges of the body. However, if the other lung would be filled with fluid and accordingly would not be available for the exchange of gases, the oxygenated blood from the breathing lung would become polluted with venous blood returning from the fluid-filled lung. The oxygen saturation of the arterial blood would thus decrease. This occurs in lobar pneumonia, where the oxygen saturation of the arterial blood usually is lowered. In pneumothorax, on the other hand, the arterial oxygen saturation usually is not depressed.

The author describes the results of the first series of 45 experiments on lavage of the lung in dogs. Pneumothorax was established on one side by inserting a trocar into the 5th or the 6th left intercostal space via a system of valves. Approximate physiological pressures were maintained in the pleural cavity during the respiratory cycle. Tracheotomy was performed in order to facilitate positioning of a special endobronchial cannula in the left main bronchus. The pneumothorax permitted intermittent collapse and expansion of the left lung independent of, and without interfering with, spontaneous respiratory excursions of the thorax. The left lung then was ventilated with oxygen in order to remove nitrogen from the air spaces which, by not being rapidly absorbed, might prevent dialyzing fluid from coming into contact with the alveolar wall. Through the endobronchial tube, Ringer's solution, to which 1.25% glucose had been added (in order to balance the osmotic effect of the plasma proteins), was permitted to flow from a reservoir into the left lung. After a certain volume had been instilled, the fluid was made to flow out of the lung via the same cannula. This was repeated several times while exchange of gases continued uninterruptedly in the other lung which breathed an oxygen-rich gas mixture.

In this manner, considerable amounts of urea and barbiturates could be removed from the body. As far as transfer of water, salts, and sugar is concerned, the properties of the "alveolar membrane" appeared to be consistent with inert semipermeability. The results obtained with serum and plasma, however, are inconsistent with such a concept. Thiocyanate was recovered in significant amounts from the fluid aspirated from the air spaces of the lung, subsequent to the intravenous injection of sodium thiocyanate. This renders support to the view that the bare walls of at least part of the alveolar capillaries are in immediate contact with the alveolar contents. Suggestions are made as to the possible application of this new method for clinical, physiological, and pathophysiological purposes.

Egg-Containing Meals and Blood Coagulation. E. Orma, D. N. Rhodes and A. Keys. Lancet 1:388-390 (Feb. 21) 1959 [London].

After test meals containing 2 eggs or 50 Gm. of butter, margarine, or hard vegetable cooking fat, O'Brien in 1956 found similar shortening in the coagulation time of recalcified plasma in the presence of Russell-viper venom (Stypven-time). Since the 2 eggs contained only 10 Gm. of glyceride fat but 3 Gm. of phospholipids, he suggested that eggs may owe their unusual activity in this respect to their large phospholipid content. Later experiments by O'Brien appeared to support this hypothesis. He observed that 2.5 Gm. of egg lecithin, which was inactive in his in vitro experiments, detectably shortened the Stypven-time when ingested; and a phospholipid mixture (comprising less than 5% of triglyceride, about 30% of lecithin, 30% of phosphatidyl ethanolamine, and 35% of inositol-containing phospholipids), when ingested in small amounts, produced a shortening of the Stypven-time which was comparable to that observed after the ingestion of 5 times as much triglyceride. His conclusion was that a part of the phospholipids was absorbed relatively unchanged, and this could explain the marked response after phospholipid-containing egg meals.

The studies described in this paper were carried out to determine whether either of the 2 main phospholipids present in eggs is responsible for the claimed activity of ingested egg fat on blood coagulation. Nine middle-aged, physically normal men (chronic schizophrenic patients in the Hastings [Minn.] State Hospital), after 10 hours' fasting, were given breakfast of dry toast and jelly, coffee, and a scramble of either (*a*) 3 whole eggs, (*b*) 3 egg whites plus the total lipids of 3 eggs (total lipid), (*c*) 3 egg whites plus the lipids of 3 eggs from which phosphatidyl ethanolamine had been removed (PE-free lipid), (*d*) 3 egg whites plus egg lipids, equal in weight to the total lipids of 3 eggs, from which all phospholipids had been removed (PL-free lipid), (*e*) 3 egg whites, or (*f*) a virtually fat-free test meal containing sucrose, rice, and nonfat milk solids providing 1,078 calories. The subjects were divided into 3 groups, and the test meals were rotated over 6 experiments conducted at weekly intervals.

It was found that the total lipid of 3 eggs (13.5 Gm.) produced a significant shortening in the coagulation time (Stypven-time) of Russell-viper venom accelerated recalcified plasma at 3½ and 4½ hours after ingestion. Removal of the total phospholipids or phosphatidyl ethanolamine from the egg lipids did not significantly alter the result. The whole-blood coagulation time (in siliconized tubes) was not significantly shortened by the ingestion of this amount of egg lipids. Thus, the results of these studies did not support the suggestion of O'Brien that the shortening of the Stypven-time after eating eggs is due to the phospholipids contained in them. The authors have no data to show whether the total lipid of eggs is more effective than an equal quantity of any other food fat, but such effect as it has is clearly not dependent upon either the total phospholipid or the phosphatidyl ethanolamine content.

PUBLIC HEALTH

Medical Aspects in the Control of Hospital-Acquired Staphylococcal Infections. K. M. Schreck. Am. J. M. Sc. 237:151-157 (Feb.) 1959 [Philadelphia].

When a hospital is confronted with hospital-acquired staphylococcic infections, the extent of the problem should be determined by tabulating all infections related to hospitalization, including those occurring in the immediate period after discharge of the patient. When an epidemic is present, all isolated coagulase-positive staphylococci should be bacteriophage typed to find the prevalent strain and to trace its possible source. Since about 1955 type 80/81 of staphylococcus organisms has been the most frequent cause of hospital epidemics, but a few other types have also been found to produce epidemics. Most important in successful control is strict isolation of infected patients and removal from duty of infected personnel. Other control measures must be decided on locally by a given hospital. The hospital's committee on infections should institute these control measures and have the authority to enforce them. Routine therapy of infections in patients and personnel does not require the use of antibiotics.

The epidemic strain of Staphylococcus 80/81 is no more resistant to germicides than is any other Staphylococcus organism. The final assessment of the value of a germicide applied to walls, floors, and blankets lies in its effect on the infection rate in a hospital. It is hoped that a governmental health agency will conduct laboratory and field trials on these preparations. More information is required before significance can be attached to the staphylococci in the inanimate environmental reservoir. Hospital-acquired staphylococcic infections will probably be a long-term problem, because the epidemic strains are passing to the community in greater numbers. This means the community will continue to reseed the hospitals with the staphylococci.

Tobacco Smoking, Respiratory Symptoms, and Ventilatory Capacity: Studies in Random Samples of the Population. I. T. T. Higgins. Brit. M. J. 1:325-329 (Feb. 7) 1959 [London].

The relation between smoking and respiratory symptoms and disability has been studied in 734 men, between the ages of 25 and 64 years, who were randomly selected from urban and rural populations, defined by private census during the course of community surveys into the prevalence of common diseases. A questionnaire was used to record respiratory symptoms and smoking habits; the ventilatory capacity was assessed, utilizing the indirect maximum breathing capacity test. A clear relation between smoking and persistent cough and sputum was invariably found; there was a marked trend of increasing cough and sputum with increasing tobacco consumption. Smokers also tended to report more chest illness, wheezing, breathlessness, and "chronic bronchitis" (defined as persistent sputum and at least one chest illness during the past 3 years) than nonsmokers. Assessment of ventilatory capacity revealed a higher mean maximum breathing capacity in nonsmokers than in smokers, the best estimate of the difference, allowing for the size of the various groups studied, being 9 liters a minute. There was, however, no significant downward trend with increasing tobacco consumption among the smokers. Most of the pipe smokers smoked less than 15 Gm. of tobacco daily. Though pipe smoking did not appear to be entirely harmless, it seemed to be much less apt than cigarette smoking to cause symptoms. One approach to the problem of tobacco addiction might be to try to persuade cigarette smokers to change to a pipe. Apart from other considerations, those persuaded would probably smoke less.

Rotary Power Lawn Mower Injury: Perforation of the Stomach. T. H. Henley. J. Oklahoma M. A. 52: 86-87 (Feb.) 1959 [Oklahoma City].

The cutting bars of rotary power lawn mowers rotate at 2,400 to 3,600 rpm, and the force of the rotating blades is estimated to be in excess of 10,000 lb. per square inch. An object struck by the blades (nails, rocks, etc.) may attain speeds in excess of 300 ft. per second. This equals the speed of many shell fragments and approaches the speed of a bullet. Immediate death from such missiles has been reported on several occasions.

A 15-year-old boy was hospitalized at 9:10 p. m. with the history that at 6 p. m. he was cutting grass with a rotary power mower when the mower struck a metal object, which hit him in the abdomen. His physician referred him to the University of Oklahoma Medical Center in Oklahoma City. He had had no nausea or vomiting, had voided clear urine, and had a normal bowel movement after the injury. There was generalized abdominal tenderness, most pronounced in the epigastrium. There was muscle guarding and rebound tenderness in the upper abdomen. Abdominal exploration revealed a 2-in. rusty nail in the anterior aspect of the body of the stomach near the lesser curvature. The nail had perforated the stomach through and through and was lying in the tract thus formed. The nail was removed, and the 2 perforations were closed. Ten thousand units of tetanus antitoxin was given after skin testing. The patient was discharged on the 5th postoperative day and had an uneventful convalescence.

The problem of power lawn mower injuries is a serious one, and physicians should call the public's attention to the dangers of these mowers. The habit of clearing the grass from the power mowers while the motor is running is certainly a very dangerous one. Lawns should be cleared of rocks, wire, etc. before they are mowed. Manufacturers of power lawn mowers should be aware of the dangers.

Current Virus Disease Problems in Minnesota. H. Kleinman. Minnesota Med. 42:75-82 (Feb.) 1959 [St. Paul].

In each of the years from 1955 to 1957 Minnesota has had experience with viral diseases of the central nervous system—diseases that were similar as to symptoms but were caused by different enteroviruses. Virus isolations effected in these years included poliomyelitis viruses of all types in 231 patients, Coxsackie B5 virus in 78 patients, enteric cytopathogenic human orphan (ECHO) type 9 virus in 120 patients, and other not yet completely identified viruses in 49 patients. The agent responsible for the viral diseases of the central nervous system occurring in 1955 was the poliomyelitis virus. In 1956, while the poliomyelitis virus was still operative, Coxsackie B5 virus was isolated more frequently than any type of poliomyelitis virus. In 1957 the predominant virus was ECHO type 9 virus, a new one for Minnesota.

The diagnostic dilemma of the practicing physician with respect to viral diseases of the central nervous system can be profound and troublesome. The season of occurrence is of no diagnostic help to him except for mumps meningoencephalitis, which tends to occur more frequently in the spring of the year well in advance of the usual poliomyelitis season. Nonparalytic poliomyelitis, Coxsackie B5 aseptic meningitis, and ECHO type 9 disease all occur during the same time of the year. In Minnesota, in 1955, poliomyelitis peaked during the first half of August; in 1956, both poliomyelitis and Coxsackie B5 meningitis peaked during the second half of August; and ECHO type 9 aseptic meningitis showed its peak during the second week of August, 1957. The age distribution curves for nonparalytic poliomyelitis and Coxsackie B5 meningitis were similar in that they showed the highest incidence in the earlier years of life. This is characteristic of a population in which childhood experience with a disease results in relative immunity for the more adult sections of that population. The attack rates of ECHO type 9 aseptic meningitis for the ages of 5 to 40 years were similar enough in magnitude to give to the curve of distribution a definite segment of plateau-like flatness. This strongly suggests that adults in Minnesota had had no previous immunizing experience with ECHO type 9 virus. Clinically, aseptic meningitis due to Coxsackie B5 virus cannot be distinguished from nonparalytic poliomyelitis by signs, symptoms, and cerebrospinal fluid findings. ECHO type 9 virus has several suggestive clinical characteristics. Foremost is the exanthem which may occur in about 30% of the patients, and the headache is often exceptionally severe.

Physicians, laboratory workers, and public health workers should be prepared to work toward a further reduction in the size of the "cause undetermined" category of virus diseases, particularly in that class known as aseptic meningitis. More emphasis will have to be placed on the need for establishing an etiological diagnosis in individual cases. Perhaps the most important guidepost for the physician is the pattern of the disease of the central nervous system which is occurring in his community. Should it be noted that there is a series of such cases occurring in a community with none of them, or a disproportionately small number of them, showing any lower motor neuron paralysis, then it is proper to infer that the disease which is occurring with major frequency is not poliomyelitis. This is the time to bend every effort toward establishing a definite etiology. From the laboratory standpoint the isolation of the offending agent in most cases can be made from the feces. Such specimens should be collected as early as possible in the course of the disease, as the chances for successful isolation decline after the first 10 to 14 days. In addition to this, paired blood samples should be submitted, the first of these drawn preferably within the first 5 days of the onset and the second drawn during the convalescent period about 2 weeks later.

Some Social and Epidemiological Aspects of Smallpox in West Bengal Including Calcutta: The Problems of Its Control and Eradication. S. K. Chattergee. J. Indian M. A. 32:89-103 (Feb. 1) 1959 [Calcutta].

During the smallpox epidemic in West Bengal, India, in 1957, 18,612 persons were attacked by the disease, and there were 10,095 deaths; in Calcutta alone, 3054 persons were attacked, and 2,056 of them died. The morbidity and mortality rates were 0.6 and 0.4 per thousand, respectively, for the entire state, and 1.1 and 0.7 per thousand, respectively, for the Calcutta municipal area. The districts of Howrah, Calcutta, Murshidabad, Malda, 24-Parganas, Hooghly, and West Dinajpur were the worst affected. The incidence of smallpox was higher in the urban than in the rural areas; the disease occurred more often in females than in males, and in persons over 10 years of age than in those aged less than 10 years. Compared with the 1956 epidemic with a morbidity rate of 0.1 per thousand and a mortality rate of 0.04 per thousand, there was a sharp increase in 1957. Cyclic exacerbations of smallpox have occurred regularly at 4-to-6-year intervals; the last preceding one occurred in 1950-1951, and 1957-1958 appears to be again a peak period of cyclic periodicity. Another factor of immediate and special importance leading to the increase in smallpox is the epidemic outbreak of the disease in neighboring states, particularly East Pakistan, with which close contacts have been maintained for social, cultural, and economic reasons.

Factors of general importance are discussed as follows. The general sanitary conditions of West Bengal have been deteriorating as the density of population has been steadily increasing. The level of immunity in the population has also deteriorated, owing to the accumulation of susceptible persons from within and outside the state of West Bengal. Because of deficient birth registration, half of the total newborn infants escape registration and, therefore, vaccination. Displaced persons migrating into the state of West Bengal, particularly from Pakistan, constitute about 26% of the total population of West Bengal, and a high percentage of nonvaccinated persons have been found among them. Because of an inadequate intelligence service, the first information of an outbreak of smallpox reaches the peripheral outpost of the local public health agencies, and that of the state, after considerable delay or when several deaths have already occurred. There has been resistance to vaccination and control of evaders.

It has to be recognized that early eradication of smallpox, in the face of existing conditions of society in India, is not a simple problem. The remedy, so far as eradication is concerned, consists in early location and isolation of the infection that is already present in West Bengal and in the vaccination of the entire population of this state for a few consecutive years. This requires an adequate intelligence service and adequate isolation arrangements, together with a favorable psychological attitude on the part of the population. For prevention of migration into West Bengal of infected and unprotected persons from without, the essentials are the framing and rigid application of appropriate legislation, an elaborate surveillance organization, a national public health campaign, and international cooperation.

BOOK REVIEWS

Atomic Medicine. Edited by Charles F. Behrens, M.D., F.A.C.R., Roentgenologist, Yater Clinic, Washington, D. C. Third edition. Cloth. $15. Pp. 705, with illustrations. Williams & Wilkins Company, 428 E. Preston St., Baltimore 2, 1959.

This book continues to be a courageous attempt to keep physicians and medical students aware of the rapidly unfolding significance of atomic energy. The new edition has been widely revised to include such developments as the fall-out effects from thermonuclear weapons, newer isotope techniques in medicine, and the advances made in our understanding of radiation effects. Atomic medicine has two diametrically opposed components, the catastrophic effects of atomic weapons and the peaceful applications of atomic energy. While both of these subjects are treated fully in this text, the book is to be valued largely for its pioneering effort in presenting the treatment of mass casualties, radioactive contamination, acute radiation sickness, and other aspects of the holocaust associated with atomic disaster.

The individual contributions making up the book vary widely in their competence and method of presentation. Alongside some timely and well-written chapters one finds sections that have become sorely outdated or which contain errors that have now survived three editions. There is a large amount of duplication and even some contradictions among the various chapters. In spite of the size and scope of the book only passing reference is made to the all-important problem of the genetic effects of ionizing radiations. However, this book should be welcomed by those concerned with making the medical profession aware of its new responsibilities in an atomic age.

A Handbook of Medical Hypnosis: An Introduction for Practitioners and Students. By Gordon Ambrose, L.M.S.S.A., and George Newbold, M.B., B.S., M.R.C.S. Forewords by William Moodie, M.D., F.R.C.P., D.P.M., and William S. Kroger, M.D. Second edition. Cloth. $6.75. Pp. 276. Williams & Wilkins Company, 428 E. Preston St., Baltimore 2, 1958.

This new edition of a handbook first published in 1956 for the British medical public is an elementary textbook of rather limited value for the beginner in medical hypnosis. Ambitious in its purpose, its coverage is sketchy and its material is poorly organized, uncritically selected, and inadequately presented. For example, in chapter 3, "The Hypnotic State and Its Phenomena," six pages are devoted to a general discussion of the hypnotic state and brief, incomplete, usually nondefinitive descriptions of some of the common phenomena of hypnosis, some of which are mentioned only by name. The rest of the chapter deals with related topics but includes such matters as a discussion of desirable personality attributes in a hypnotist.

The chapters on clinical topics are also inadequate. For example, beginning on page 77 the medical history of a patient with mucous colitis is given, including the negative laboratory findings in 1951, the x-ray report then, and the details of the operation in 1952, but the details of hypnotherapy in 1954 are limited to the statement on page 80 that "treatment took place from the 9th of March until the 1st of June and comprised fifteen visits," and the statement that the patient was hypnotized on the first visit. In addition, four unhappy memories of the patient are briefly cited. On pages 201 and 202 the hypnotherapy of a patient with functional uterine bleeding is described thus: "During the course of a few sessions the reason for the symptoms was explained to the patient and the whole situation 'worked through' under hypnosis (for she was a good hypnotic subject)." References for further reading are scattered throughout the book but these are repetitious, poorly selected, and often no more than general medical references. This book is not recommended.

Cranio-Cerebral Topometry in Man: Location and Variation in Position of Cerebral Subcortical Structures with Special Reference to Neurology, Neurosurgery, and Neuroradiology. Par A. Delmas, professeur d'anatomie fonctionnelle et de neuroanatomie à la Faculté de médecine de Paris, et B. Pertuiset, neuro-chirurgien des hôpitaux de Paris. Avec la collaboration de M. H. Pineau pour la partie statistique. [In French and English.] Cloth. $38.50. Pp. 436, with illustrations. Charles C Thomas, Publisher, 301-327 E. Lawrence Ave., Springfield, Ill.; Masson & Cie, 120 boulevard Saint-Germain, Paris 6e, France; Blackwell Scientific Publications, Ltd., 24-25 Broad St., Oxford, England; Ryerson Press, 299 Queen St., W., Toronto 2B, Canada, 1959.

Recent work on experimental animals has demonstrated the wide diversity and fine localization of function of the deeper structures in the cerebrum. The possibility of abolishing otherwise intractable pain by placing small lesions electrically in the brain is but one of many prospective applications of this work, and it depends on the use of stereotaxic instruments for the correct placement of electrodes. The present work by Delmas and Pertuiset presents additional data concerning the topography of cerebral structures and their variations in position. An introductory part explains terminology and

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techniques. The second part is an alphabetically arranged list of structures, each entry being accompanied by descriptive text and a systematic indication of the location of the given structure in the atlas which constitutes the third part of the book. This part is a series of life-sized photographs of sections of the brain with its bony case. In one group the plates are of sagittal and parasagittal sections; in a second group, of frontal sections; and in a third, of horizontal sections. On each page facing a given photograph there is a well-labeled diagram pointing out the essential structures. The fourth part is a statistical presentation of the variations in volume and position of the subcortical structures. The fifth part is a discussion of the utility and significance of craniocerebral topometry, and the book ends with an alphabetical index, a bibliography, and a table of contents.

The text is printed in parallel columns of French and English, and the labeling of the diagrams is in the Latin of the PNA (Parisiensa Nomina Anatomica) of 1955. All three languages are handled magnificently, and no errors are to be found. This is a priceless work of permanent value and will be essential to everyone working in the fields of neuroanatomy and neurosurgery.

Recent Advances in Respiratory Tuberculosis. By Frederick Heaf, C.M.G., M.A., M.D., David Davies Professor of Tuberculosis, Welsh National School of Medicine, Cardiff, and N. Lloyd Rusby, M.A., D.M., F.R.C.P., Physician to London Hospital, London. Fifth edition. Cloth. $8. Pp. 284, with 20 illustrations. Little, Brown & Company, 34 Beacon St., Boston 6; J. & A. Churchill, Ltd., 104 Gloucester Pl., Portman Sq., London, W. 1, England, 1959.

This new edition appears after a lapse of 10 years, resulting in profound changes in the control and management of respiratory tuberculosis and a consequent reduction in mortality in almost all parts of the world. Complacency, however, has no place if eradication of tuberculosis is considered on a global and not merely on a national basis. The international problem marks a notable development in the modern approach to the disease, and this was constantly before the authors when they prepared this revision. Their aim has been to review the subject in the light of recent work without hesitating to discuss controversial issues. The new developments in almost every branch of the subject have necessitated a complete rewriting of the book. Help and guidance was drawn from many quarters.

The 13 chapters cover epidemiology, prevention, tuberculin and tuberculin testing, BCG inoculation, chemotherapy, collapse therapy, treatment by resection, primary tuberculosis, respiratory function studies, chest radiography, rehabilitation, miscellaneous advances, definitions, classifications, statistics, and recent legislation. It is a compact, well-prepared, simple textbook, well documented and as good and comprehensive a presentation of the subject as the size of the volume permits. It should be useful to students, residents, and physicians in general who cannot and need not refer to the more comprehensive texts. It has the advantage of being prepared by qualified British authors who are authorities on their subject.

Florence Sabin: Colorado Woman of the Century. By Elinor Bluemel. Cloth. $5.50. Pp. 238, with illustrations. University of Colorado Press, Boulder, 1959.

Each section of this book shows the late Dr. Sabin in a different environment and a new light. The first, entitled "Early Beginnings," is most likely to interest readers who enjoy picturing life in the America of the 1870's and 1880's. The second is devoted to the Johns Hopkins University period and describes the experiences of a woman student in a new medical school where important funds were donated by women while the curriculum was still considered by most people as something for men only. The third describes the period of research at the Rockefeller Institute, and the fourth covers her life in Denver, where her earnest concern with problems of public health, together with the desires of the public to heap honors on her, prevented the intended life of retirement. The fifth section describes the declining period after her 80th birthday.

The reader is inevitably impressed and inspired by the recital of this extraordinary story and by the endless variety and broadness of the experiences that become part of any life devoted to medical science. Florence Sabin had not one career but several, and in each she maintained contact with realities. There is something in this book for every reader. The scientist may wish there had been more technical detail about her researches, but what the book may lack in this respect is made up for by a good bibliography, an index, and many other proofs of the author's competence and diligence.

Bone Tumors. By Louis Lichtenstein, M.D., Chief Pathologist, General Medical and Surgical Hospital, Veterans Administration Center, Los Angeles. Second edition. Cloth. $12. Pp. 402, with 220 illustrations. C. V. Mosby Company, 3207 Washington Blvd., St. Louis 3, 1959.

The author has organized his subject matter well and has presented some pertinent remarks, aimed at the physician, in regard to the diagnosis and management of patients with bone disease. The discussion on nonneoplastic lesions of bone which may be mistaken for tumors is a valuable addition to the subject. As the entire subject is treated by the author alone, and as he is a pathologist, the sections on clinical findings and treatment are inadequate. This is partially corrected by adequate reference lists.

QUESTIONS AND ANSWERS

OBESITY

To the Editor:—*Can obesity be treated without restricting the caloric intake? An obese patient was placed on a diet and therapy with amphetamine, thyroid extract, aloin, and phenobarbital. She would not restrict her diet and lost little weight. Now she has found a physician who tells her to eat and she says she eats just as much as she ever did. To the amazement of her husband, she has lost 51 lb. (23.1 kg.) in three and one-half months and has no complaints. Her physician gives her white capsules to take with her meals. Sometimes she takes, in addition, an uncoated brown tablet, larger than aspirin, once a day. The physician sees her every two weeks and each time gives her a subcutaneous or intramuscular injection of fluid that looks like skimmed milk. He has many patients in his treatment room, and each one sees the others being weighed and examined. He gives them an adequate examination. The visit, capsules, and injection cost each patient $5 every two weeks. Please give information as to how weight may be reduced without restriction of the caloric intake.*

Fred Mather, M.D., Brooklyn, N. Y.

Answer.—This consultant is not aware of any effective reducing plan recognized by nutrition authorities in the United States that permits the unlimited intake of calories. Psychogenic and genetic factors play a limited rôle, but the basic cause of obesity is an intake of more calories per day than are expended, the remainder accumulating as fat. The pamphlet entitled "The Healthy Way to Weight Loss," published by the Council on Foods and Nutrition of the American Medical Association, describes in simple language the principles behind weight reduction. This pamphlet might be recommended to the patient presented in the question.

CHEMICAL BURNS

To the Editor:—*What is the present status of the use of neutralization treatment for acid or alkali burns of the skin both as emergency treatment and later?*

Philip A. Fuqua, M.D., Richland, Wash.

Answer.—It is important to remove as much of the acid or alkali as quickly as possible after exposure and to follow this with appropriate neutralization. The emergency treatment, however, will depend to a certain extent on the particular action of the irritant itself. The burns caused by concentrated acids are usually not as extensive as those caused by alkalis. For the emergency treatment of acid burns, immediately wash with water and follow with a 0.5% sodium bicarbonate solution. The follow-up treatment will depend on whether it is a first, second, or third degree burn. The further use of alkali, however, is not necessary. For the emergency treatment of alkali burns, it is important to know the chemical nature of the alkali causing the burn. Here too, it is important to remove the irritant as quickly as possible by liberal use of water. If there is exposure to calcium oxide or quick lime, removal of the irritant with water must be done in a particular way. Because the heat of solution of a single grain of calcium oxide is over 18,000 calories, all solid particles should be removed before the lime is wetted. If water is used at all, a stream of water must be applied under pressure, which will remove most of the particles before they become wet. As a rule, after alkali burns are washed with water they should be washed with a 1% acetic acid solution. The follow-up treatment will also depend on the extent of the burn and the chemical producing it. Once the emergency treatment is given, acid ointments are not needed in the follow-up treatment.

BODY CHEMISTRY AFTER DEATH

To the Editor:—*Faced with the problem of determining whether a patient has died in diabetic acidosis, how can one estimate the changes which occur after death in the chemistry of body fluids? A diabetic whose body was examined 12 hours after death (having been refrigerated) showed a ventricular cerebrospinal fluid sugar level of 56 mg. per 100 ml. and carbon dioxide combining power of the same fluid of 5.3 mEq. per liter. Urine and blood were unobtainable. Are there any references to normal values of body fluid chemistries at various intervals after death?*

M.D., Illinois.

Answer.—Postmortem determination of the cerebrospinal fluid sugar or serum glucose values would probably not be of any value in spite of refrigeration. Taken immediately after death they might reflect hyperglycemia, but bacterial decomposition and tissue fluid dilution would soon make these determinations useless. Results of carbon dioxide combining power determinations are quickly af-

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fected due to diffusion of tissue juices and agonal hypoxia and hypercapnia. Serum sodium potassium and chloride determinations presumably would be accurate for at least 30 to 60 minutes after death and, perhaps, several hours with refrigeration. Figures regarding chemical determinations after death can be obtained from the standard textbooks on medicolegal medicine.

TREATMENT OF SNAKE BITE

To the Editor:—*In* The Journal, *Feb. 14, 1959, page 782, the question of sources of supply of coral snake antivenin is raised. Charity Hospital of Louisiana, New Orleans, stocks coral snake antivenin. It is obtained from C. Amaral and Cia, L. T. D. A., Gloria 34, P. O. Box 2123, São Paulo, Brazil. Cobra antivenin, both Indian and African, is also stocked. Since 1955, three cobra bites and one coral snake bite have been treated at Charity Hospital. In addition, coral snake antivenin has been supplied to neighboring cities on two occasions.*

Adolph Flores, M.D.
Charity Hospital
New Orleans.

To the Editor:—*A brief account of the results of certain laboratory studies, hitherto unpublished, may be of interest in connection with the letter on treatment of snakebite, which appeared in* The Journal, *Feb. 14, 1959, p. 782. No antivenin specific for coral envenomation is generally available in the United States. A serum produced with cobra venom cannot properly be called a "coral antivenin." Although it is true that both Naja (cobra) and Micrurus (coral snake) are members of the family Elapidae and both bear neurotoxic venom, this is no reason to assume that both venoms contain the same toxic fractions.*

Little is known about the neurotoxins in any venom. Data are particularly scant on the composition of Micrurus venom, since it is so difficult to obtain. Limited studies were made in the Wyeth biological laboratories on a small quantity of Micrurus venom that Ross Allen, of Silver Springs, Fla., was able to furnish in 1950. The results indicated that the neurotoxins in Micrurus venom and those of two species of Naja (cobra) are not the same. Results of neutralization tests run with Micrurus fulvius venom and various serums are as follows: (1) Pasteur C serum (Naja or Asiatic cobra), lot 1 neutralized 0.04 mg. (3.0 LD_{50}*) of Micrurus fulvius venom; (2) South African Anti-Cape serum (N. flava or S. African cobra) from South African Institute for Medical Research, Johannesburg, lot 3 neutralized 0.05 mg. (3.75* LD_{50}*) of Micrurus fulvius venom; (3) antivenin (Crotalidae) Wyeth, pool 6—neutralized 0.05 mg. (3.75* LD_{50}*) of Micrurus fulvius venom; (4) antivenin (Crotalidae) Wyeth, pool 6, and Pasteur C serum, lot 1 (combined, equal parts) neutralized 0.05 mg. (3.75* LD_{50}*) of Micrurus fulvius venom; (5) normal horse serum (unpreserved) neutralized 0.04 mg. (3.0* LD_{50}*) Micrurus fulvius venom; and (6) normal horse serum (preserved) neutralized 0.04 mg. (3.0* LD_{50}*) Micrurus fulvius venom.*

Any protein or animal body will nullify a certain amount of venom. The indications are that any beneficial results from administration of cobra antiserum or antivenin (Crotalidae) to a victim of Micrurus envenomation probably would be of a nonspecific nature. Some medical authorities have maintained for a number of years that mechanical measures (tourniquet, incision, and suction) are useless for cobra envenomation and, hence, would probably be equally valueless for poisoning by Micrurus. The various known sources of antivenins for snake, scorpion, and spider envenomation are listed in the article by Keegan (Venoms, Washington, D. C., American Association for the Advancement of Science, publication 44, 1956, pp. 413-438). Several cobra antiserums produced in various countries are listed. The only serum produced with Micrurus venom—Soro Anti-Elapidico—is listed by Instituto Butantan. Other sources may have become available since this article was prepared in 1954.

Eleanor E. Buckley
Wyeth Laboratories
Philadelphia 1.

HYPNOSIS MACHINE

To the Editor:—*This is in reference to the Question and Answer entitled "Hypnosis Machine" which appeared in* The Journal, *March 21, 1959, page 1402. I have had an opportunity to examine the article that was mentioned at the end of the reply and find that it is based on incorrect theoretical electroencephalographic conclusions. The following statement is quoted from that article: "A slowing down of the alpha rhythm is indicative of a sleep-like state. Experimentally, these cortical and subcortical changes could be utilized to signal the onset of hypnosis." Actually, the alpha rhythm, with rare exceptions, does not slow down. It decreases in amplitude when an individual falls asleep and finally drops out. It thus could be utilized, although with reservations, to signal the onset of sleep but not of hypnosis. I believe that the promotion-like discussion of this "machine" that appeared in the consultant's reply to the inquiry is completely unjustified.*

Harold Rosen, M.D., Chairman
Committee on Hypnosis
A. M. A. Council on Mental Health
1101 N. Calvert St.
Baltimore 2.

WASHINGTON NEWS

Senate Hearings on Keogh Bill . .

Experts Testify on Problems of Aged . .

Administration Against Higher Public Health Outlays . .

Health Insurance for U. S. Workers . .

Miscellany . .

SENATORS HEAR VIEWS ON THE KEOGH BILL

Spokesmen for the American Medical Association and scores of other professional organizations appeared before the Senate Finance Committee to urge approval of the House-cleared measure that would encourage the self-employed to invest in pension plans through tax deferrals.

Dr. George M. Fister of Ogden, Utah, a member of the A. M. A. Board of Trustees and Chairman of the A. M. A. Council on Legislative Activities, told the committee the bill, among other things, would help "make the smaller communities of America better able to compete with the big cities for the services of physicians." Dr. Fister was accompanied by Dr. Vincent W. Archer of Charlottesville, Va., a member of the A. M. A. House of Delegates and of the A. M. A. Committee on Federal Medical Services.

The first witness at the hearings, David A. Lindsay, assistant to the Treasury Secretary, renewed the administration's opposition to the legislation. He said it would cost the government 365 million dollars a year in revenue. However, the official said that "the Treasury recognizes that present law does not give self-employed persons tax treatment for their retirement savings comparable to that now accorded to employes covered by employer-financed pension plans." He conceded that "employee pension plans, if arranged on a non-discriminatory basis, [would] receive favorable tax treatment."

Dr. Fister declared that "unless something is done to make self-employment as financially attractive as employee status, we believe that there is a real danger that many professional men will bypass the private practice of their profession.

"With high taxes and inflated living costs, it is difficult for the self-employed person to set aside adequate funds for retirement without a tax deferment similar to that available to corporate employes," he testified. "By extending the tax deferment privilege to the country's 11 million self-employed, this legislation will give them an opportunity during their best earning years to save for their old age."

Asserting that a shift away from individual enterprise has become noticeable in the past few years, Dr. Fister said a continuation of the present situation "could contribute to a maldistribution of physicians since it makes the large city more attractive to the young professional man by providing more opportunities for him to become employed.

"On the basis of my own observations over many years of practice in medicine, I am convinced that this is one of the factors contributing to the pronounced migration of professional people into urban areas. So, quite apart from the objective of obtaining tax equality with our employed counterparts, we urge you to approve legislation of this type, because it is in the public interest."

The measure before the committee would allow tax deferrals for self-employed persons of up to 10% of adjusted gross income annually, with a maximum of $2,500, on money set aside in qualified retirement or pension programs. The bill, sponsored in the House by Rep. Eugene J. Keogh (D., N. Y.) and Rep. Richard M. Simpson (R., Pa.), won overwhelming approval in the House early this session.

SENATE HEARINGS ON AGED

A special Senate subcommittee opened a sweeping investigation of problems of the aging with three days of testimony from experts in the fields of medicine, economics, employment, housing, and mental health.

One of the first witnesses before the subcommittee, headed by Sen. Pat. McNamara (D., Mich.), was Dr. Frederick C. Swartz, Chairman of the American Medical Association Committee on Aging.

In introducing Dr. Swartz, the subcommittee chairman said he was pleased that the A. M. A. has taken such interest in the panel's work, "and certainly we need their [physicians] cooperation."

Dr. Swartz declared that the A. M. A. Committee's studies "showed that the health of the senior citizen is not solely a medical or health habits matter." Socioeconomic and psychological factors, he said, "prevent many persons from exercising their potential for responsible participation in society.

"As long as these patterns exist, unnecessary illness will occur despite medical care and otherwise sound health programs," Dr. Swartz said. "Likewise, the duration of illnesses may be unnecessarily prolonged, the degree of disabilities increased."

The A. M. A. Committee's goal of "optimum health of each individual" in the aged group was outlined to the subcommittee by Dr. Swartz. It embraces, he noted, adequate medical care at the lowest practical cost for the ill; promotion of better understanding and wider use of restorative services on behalf of the disabled; encouragement of group and individual activities for the prevention of illness among the elderly, and "the promotion of long-range positive health programs which will increase the over-all capacities of persons to live active, meaningful lives in their later years."

(Continued on next page)

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Lown, B., and Levine, S. A.:
Current Concepts in Digitalis Therapy, Boston,
Little, Brown & Company, 1954, p. 23, par. 2.

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Other panelists who discussed health problems included Wilbur Cohen, professor of social welfare at the University of Michigan and special consultant to the subcommittee; Dr. Maurice Linden, director of the Philadelphia public health department's mental health division, and Dr. Murray Ferderber, chairman of the Pennsylvania commission on restorative medical services. Dr. Howard Rusk of New York University–Bellevue Medical Center was not present but submitted a statement.

All of the witnesses agreed that the problems of the aged and aging are complicated and much broader than mere physical illness. For example, Dr. Linden said that mental problems are one of the major difficulties in a "youth-oriented country." He called for changes in the public attitude toward the elderly, noting that in some other countries the aged traditionally have been held in high respect.

In an opening statement, Senator McNamara said, "in my opinion the good health, and the income to sustain it, of 15 million Americans over 65 *is the most vital problem in this field of increasing* national concern."

Other members of the subcommittee of the Senate Labor and Public Welfare Committee are Jennings Randolph (D., Va.), Joseph Clark (D., Pa.), Everett Dirksen (R., Ill.), and Barry Goldwater (R., Ariz.).

FLEMMING OPPOSES NEW GRANTS FOR PUBLIC HEALTH SCHOOLS

Arthur S. Flemming, Secretary of Health, Education, and Welfare, asked Congress to turn down measures authorizing new federal public health programs. He told a House commerce subcommittee that the legislation would establish a permanent program of federal subsidization without legislative safeguards to insure that the funds would be used to strengthen or improve training services rather than to replace existing sources of financial support.

The administration official also said enactment would establish precedents with potentially far-reaching implications for general federal support of all universities and colleges.

The measure at issue would provide 6 million dollars annually for grants to public health schools, authorize 15 million dollars over five years for construction grants to the schools, provide 1 million dollars' worth of grants to schools for public health training of nurses, and authorize 3 million dollars annually for grants to states for local public health work. The most controversial section would authorize a five-year program "with such sums as Congress may determine" to cover the costs of traineeships for graduate or special training in public health for physicians, engineers, nurses, and other public health personnel.

At the same time, Flemming endorsed provisions to extend the current programs of federal aid for training of professional public health personnel and for advanced training of professional nurses. These are the major provisions of a bill that has been tentatively approved by the Senate Labor and Public Welfare Committee.

Most of the witnesses before the House commerce subcommittee headed by Rep. Kenneth Roberts (D., Ala.) disagreed with Flemming's position, and endorsed the expanded aid proposals. Many of the witnesses were officials of public health schools.

FEDERAL EMPLOYEES HEALTH INSURANCE BILL DRAFTED

Legislation giving the Civil Service Commission broad leeway in the establishment of a voluntary health insurance program for United States workers was introduced by Sen. Richard Neuberger (D., Ore.) and Sen. Olin Johnston (D., S. C.).

Senator Neuberger is chairman of a Senate post office and civil service subcommittee that held hearings earlier this year on proposals to provide a contributory health insurance plan for civilian federal workers that would be similar to those now used in many industries. Senator Johnston is chairman of the full committee.

Despite the lawmakers' action, the committee had not approved a health insurance measure as of this writing, and meetings were being held with administration officials in efforts to compromise differences. However, it was expected that the measure that will clear the committee would in general follow the Neuberger-Johnston bill. Hearings have not been held so far on the issue in the House.

Premiums would be fixed under the legislation—up to $1.75 every two weeks for single employees and $4.25 for workers with dependents—and the government would match the contributions. However, benefits would not be fixed, depending instead on the amount of money in the fund.

Up to 120 days of hospitalization is provided in the measure, though this also would depend on the fiscal setup of the plan; the surgical benefits would be on the basis of "reasonable, necessary, and customary charges . . ." and the plan would pay 80% of charges for major medical care up to $1,500, after a deduction of $100, and 100% of costs above $1,500.

The commission would be authorized to provide alternative benefits which could include deductible and coinsurance provisions.

Cost of the measure was estimated at about 300 million dollars annually to the government, compared with the administration's proposed maximum of 210 million dollars. An estimated 1,800,000 civilian workers and their 2,700,000 dependents would be eligible for the insurance.

MISCELLANY

The Food and Drug Administration has again called drug manufacturers' attention to the requirement that "sustained release" drugs be pretested for safety even though the contents would be safe in regular form. The agency noted that "sustained release" drugs—those with special coatings designed to release doses in the system at specified intervals—are being used with increasing frequency. The notice to manufacturers, FDA said, is aimed at providing "additional protection of consumers from overdosage caused by too rapid release of active ingredients or lack of benefit caused by failure of a tablet to disintegrate fast enough."

The Department of Agriculture reported that 90% or more of radioactive contamination can be removed from farm land by raking off straw mulch, removing sod, or scraping off 2 to 3 in. of soil. Rolling contaminated land or spraying it with asphalt had little effect on contamination, according to the department.

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MEETINGS

AMERICAN MEDICAL ASSOCIATION: Dr. F. J. L. Blasingame, 535 North Dearborn St., Chicago 10, Executive Vice-President.
1959 Clinical Meeting, Dallas, Texas, Dec. 1-4.
1960 Annual Meeting, Miami Beach, Fla., June 13-17.
1960 Clinical Meeting, Washington, D. C., Nov. 29-Dec. 2.
1961 Annual Meeting, New York City, June 26-30.
1961 Clinical Meeting, Denver, Nov. 28-Dec. 1.

AMERICAN

1959

June

Intermountain Pediatric Society, Sun Valley, Idaho, June 26-28. Dr. J. R. Newton, Memorial Medical Center, 2000 S. 9th E., Salt Lake City, Utah, Publicity Chairman.

July

American Society of Facial Plastic Surgery, New York City, July 17. Dr. Samuel M. Bloom, 123 E. 83rd St., New York 28, Secretary.

American Society of X-ray Technicians, Shirley Savoy Hotel, Denver, July 4-9. Miss Genevieve J. Eilert, 16 14th St., Fond du Lac, Wis., Executive Secretary.

Oregon Cancer Conference, University of Oregon Medical School, Portland, July 16-17. Dr. Martin A. Howard, 1115 S. W. Taylor St., Portland 5, Ore., Chairman.

Rocky Mountain Cancer Conference, Brown Palace Hotel, Denver, July 22-23. Dr. N. Paul Isbell, 835 Republic Bldg., Denver 2, Chairman.

August

American Congress of Physical Medicine and Rehabilitation, Hotel Leamington, Minneapolis, Aug. 30-Sept. 4. Miss Dorothea C. Augustin, 30 N. Michigan Ave., Chicago 2, Executive Secretary.

American Dietetic Association, Statler Hilton, Los Angeles, Aug. 25-28. Miss Ruth M. Yakel, 620 N. Michigan Ave., Chicago 11, Executive Secretary.

American Hospital Association, Statler Hotel, New York City, Aug. 24-27. Dr. Edwin L. Crosby, 18 E. Division St., Chicago, Director and Secretary.

American Veterinary Medical Association, Hotel Muehlebach, Kansas City, Mo., Aug. 24-28. H. E. Kingman Jr., D.V.M., 600 S. Michigan Ave., Chicago 5, Executive Secretary.

Biological Photographic Association, Inc., Sheraton-Mount Royal Hotel, Montreal, Canada, Aug. 31-Sept. 3. Miss Jane H. Waters, Box 1668, Grand Central P. O., New York 17, Executive Secretary.

National Medical Association, Detroit, Aug. 10-13. Dr. John T. Givens, 1108 Church St., Norfolk, Va., Secretary.

Nevada State Medical Association, Reno, Aug. 19-22. Dr. Gilbert G. Lenz, 505 S. Arlington Ave., Reno, Nev., Chairman.

Northwest Proctologic Society, Timberline Lodge, Mount Hood, Ore., Aug. 26-29. Dr. John L. McKay, 645 Medical Dental Bldg., Seattle 1, Secretary-Treasurer.

Rocky Mountain Radiological Society, Shirley-Savoy Hotel, Denver, Aug. 20-22. Dr. John H. Freed, 4200 E. Ninth Ave., Denver 20, Secretary-Treasurer.

Society for Clinical and Experimental Hypnosis, Fairmont Hotel, San Francisco, Aug. 3-5. Dr. Irving Schwartz, 2340 Sutter St., San Francisco 15, Chairman, Program Committee.

Southeastern Oklahoma Clinical Symposium, McAlester Clinic, McAlester, Aug. 8-9. Mr. Charles A. Miller, McAlester Clinic, McAlester, Okla., Business Manager.

West Virginia State Medical Association, The Greenbrier, White Sulphur Springs, Aug. 20-22. Mr. Charles Lively, P. O. Box 1031, Charleston 24, Executive Secretary.

September

American Association of Medical Clinics, Sheraton-Blackstone Hotel, Chicago, Sept. 24-26. Dr. Edwin P. Jordan, Box 58, Charlottesville, Va., Executive Secretary.

American Association of Obstetricians and Gynecologists, The Homestead, Hot Springs, Va., Sept. 10-12. Dr. E. Stewart Taylor, 4200 E. Ninth Ave., Denver 20, Secretary.

American Association for the Surgery of Trauma, Mount Washington Hotel, Bretton Woods, N. H., Sept. 24-26. Dr. William T. Fitts Jr., 3400 Spruce St., Philadelphia 4, Secretary.

American College of Gastroenterology, Biltmore Hotel, Los Angeles, Sept. 19-26. Mr. Daniel Weiss, 33 W. 60th St., New York 23, N. Y., Executive Director.

American College of Surgeons, The Traymore Hotel, Atlantic City, N. J., Sept. 28-Oct. 2. Dr. Paul R. Hawley, 40 E. Erie St., Chicago 11, Director.

American College of Surgeons, Ohio Chapter, Statler Hotel, Cleveland, Sept. 11-12. Dr. Berton M. Bogle, 311 S. Market, Troy, Ohio, Secretary-Treasurer.

American Roentgen Ray Society, The Netherland Hilton Hotel, Cincinnati, Sept. 22-25. Dr. C. Allen Good, Mayo Clinic, Rochester, Minn., Secretary.

American Society of Clinical Pathologists, The Palmer House, Chicago, Sept. 7-11. Mr. Claude E. Wells, 2052 N. Orleans, Chicago 14, Executive Secretary.

Central Association of Obstetricians and Gynecologists, Drake Hotel, Chicago, Sept. 24-26. Dr. Edwin J. DeCosta, 104 S. Michigan Ave., Chicago 3, Secretary.

College of American Pathologists, The Palmer House, Chicago, Sept. 6. Dr. Arthur H. Dearing, Suite 2115, Prudential Plaza, Chicago 1, Executive Director.

Colorado State Medical Society, Brown Palace and Shirley Savoy Hotels, Denver, Sept. 8-11. Mr. Harvey T. Sethman, 835 Republic Bldg., Denver 2, Executive Secretary.

International College of Surgeons, Tennessee Section, Chattanooga, Sept. 28-29. Dr. William G. Stephenson, Medical Arts Bldg., Chattanooga, Tenn., Regent.

Kentucky State Medical Association, Columbia Auditorium, Louisville, Sept. 22-24. Mr. Joseph P. Sanford, 1169 Eastern Pkwy., Louisville 17, Ky., Executive Secretary.

Maryland, Medical and Chirurgical Faculty of the State of, Semiannual Meeting, Ocean City, Sept. 18. Mr. John Sargeant, 1211 Cathedral St., Baltimore 1, Executive Secretary.

Medical Progress Assembly, Tutwiler Hotel, Birmingham, Ala., Sept. 13-15. Dr. Herbert H. Thomas, 920 S. 19th St., Birmingham, Ala., Chairman, Publicity Committee.

Michigan State Medical Society, Pantlind Hotel, Grand Rapids, Sept. 28-29, Oct. 1-3. Mr. William J. Burns, 606 Townsend St., Lansing 15, Mich., Executive Secretary.

Mid-Continent Psychiatric Association, Holiday Inn Motor Hotel, St. Louis County, Mo., Sept. 18-20. Dr. W. Payton Kolb, Baptist Medical Arts Bldg., Little Rock, Ark., Secretary.

Montana Medical Association, Finlen Hotel, Butte, Sept. 17-19. Mr. L. Russell Hegland, 1236 N. 28th St., Billings, Mont., Executive Secretary.

National Recreation Congress, Morrison Hotel, Chicago, Sept. 28-Oct. 2. Mr. Jesse Reynolds, Department of Recreation and Parks, The Mosque, Laurel and Main Streets, Richmond 20, Va., Chairman.

North American Federation, International College of Surgeons, Chicago, Sept. 13-17. For information write the Secretariat, 1516 Lake Shore Dr., Chicago 10.

Oregon State Medical Society, Medford Hotel, Medford, Sept. 23-25. Mr. Roscoe K. Miller, 1115 S. W. Taylor St., Portland 5, Ore., Executive Secretary.

Tennessee Valley Medical Assembly, Chattanooga, Tenn., Sept. 28-29. Dr. Guy M. Francis, 109 Medical Arts Bldg., Chattanooga 2, Tenn., Chairman.

United States Section, International College of Surgeons, Palmer House, Chicago, Sept. 13-17. Dr. Ross T. McIntyre, 1516 Lake Shore Dr., Chicago 10, Executive Secretary.

Utah State Medical Association, Hotel Utah Motor Lodge, Salt Lake City, Sept. 16-18. Mr. Harold Bowman, 42 S. 5th East, Salt Lake City 2, Executive Secretary.

Washington State Medical Association, Olympic Hotel, Seattle, Sept. 13-16. Mr. Ralph W. Neill, 1309 Seventh Ave., Seattle 1, Executive Secretary.

World Medical Association, Montreal, Canada, Sept. 7-12. Dr. Louis H. Bauer, 10 Columbus Circle, New York 19, Secretary-General.

October

Academy of Psychosomatic Medicine, Sheraton-Cleveland Hotel, Cleveland, Oct. 15-17. For information write: Dr. Bertram B. Moss, Suite 1035, 55 E. Washington St., Chicago 2, Secretary.

American Academy of Ophthalmology and Otolaryngology, The Palmer House, Chicago, Oct. 11-16. Dr. William L. Benedict, 15 Second St., S. W., Rochester, Minn., Executive Secretary.

American Academy of Pediatrics, The Palmer House, Chicago, Oct. 5-8. Dr. E. H. Christopherson, 1801 Hinman Ave., Evanston, Ill., Executive Secretary.

American Association of Medical Assistants, Benjamin Franklin Hotel, Philadelphia, Oct. 16-18. Mrs. Stella Thurnau, 510 N. Dearborn, Room 924, Chicago 10, Executive Secretary.

American Association of Medical Record Librarians, Radisson Hotel, Minneapolis, Oct. 12-15. Miss Margaret G. Scully, 510 N. Dearborn St., Chicago 10, Director.

American College of Chest Physicians, 25th Anniversary Homecoming Meeting, Albuquerque, N. M., Oct. 14-17. Mr. Murray Kornfeld, 112 E. Chestnut St., Chicago 11, Executive Director.

American College of Preventive Medicine, Hotel Ambassador, Atlantic City, N. J., Oct. 21-22. Dr. John J. Wright, P. O. Box 1267, Chapel Hill, N. C., Secretary-Treasurer.

American Heart Association, Trade and Convention Center, Philadelphia, Oct. 23-27. Mr. William F. McGlone, 44 E. 23rd St., New York 10, Secretary.

American Medical Writers' Association, Chase Hotel, St. Louis, Oct. 2-3. Dr. Harold Swanberg, 510 Maine St., Quincy, Ill., Secretary.

American Otorhinologic Society for Plastic Surgery, Inc., Conrad Hilton Hotel, Chicago, Oct. 11. Dr. Joseph G. Gilbert, 75 Barberry Lane, Roslyn Heights, N. Y., Secretary.

American Psychiatric Association, Detroit Divisional Meeting, Hotel Statler, Detroit, Oct. 29-31. Dr. Benjamin Jeffries, 16321 Mack Ave., Detroit 24, Co-Chairman, Planning Committee.

American Public Health Association, Convention Hall, Atlantic City, N. J., Oct. 19-23. Dr. Berwyn F. Mattison, 1790 Broadway, New York 19, N. Y., Executive Director.

American School Health Association, Claridge Hotel, Atlantic City, N. J., Oct. 18-23. Dr. A. O. DeWeese, 515 E. Main St., Kent, Ohio, Executive Secretary.

American Society of Anesthesiologists, Inc., Americana Hotel, Bal Harbor, Fla., Oct. 5-9. Mr. John W. Andes, 188 W. Randolph St., Room 1101, Chicago 1, Executive Secretary.

American Society of Facial Plastic Surgery, Chicago, Oct. 15-17. Dr. Samuel M. Bloom, 123 E. 83rd St., New York 28, Secretary.

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PROGNOSIS AFTER MITRAL COMMISSUROTOMY

FACTORS AFFECTING RESULTS IN NINETY-TWO PATIENTS

Irving J. Adatto, M.D.
and
Harry A. Bliss, M.D., Chicago

Factors of possible value in determining whether a patient was likely to benefit from mitral commissurotomy by the closed-heart technique were sought in a series of 92 consecutive cases. The patients were repeatedly observed by the same group of physicians for as long as eight years after operation. Deaths immediately after operation or occurring during the years of observation brought the total mortality to 28%. Improvement sufficient to promote the patient at least to the next higher functional classification occurred for at least one year in 76% of the patients but was sustained during the remainder of the observation period in only 47%. The two major factors adversely affecting prognosis were preexisting mitral insufficiency and production of an inadequate valve opening at operation. Criteria for operability by this procedure are defined. New techniques of operation may be helpful to patients not meeting these criteria.

THE AVAILABILITY of open-heart surgical techniques in many centers requires a critical attempt to balance the anticipated advantages and hazards of these direct-vision procedures against the accumulated experience with closed-heart surgery. In the case of mitral stenosis, there is a continuing need for long-term studies of the effect of mitral commissurotomy on prognosis. We have observed a consecutive series of these patients for several years after operation. This report outlines their clinical course and points out factors important in the choice of an operative procedure for patients with mitral valve disease in the modern era of open-heart surgery.

Material and Methods

The material for this study consists of 92 patients who were subjected to mitral commissurotomy at the University of Illinois Research and Educational Hospitals from 1951 to November, 1957. Sixty-three were females. Ages ranged from 24 to 59 years, with an average of 39; 15 (16%) were between 21 and 30, 38 (41%) between 31 and 40, 31 (34%) between 41 and 50, and 8 (9%) between 51 and 60.

From the Research and Educational Hospitals and the Department of Medicine, University of Illinois.

Prior to operation, each patient was admitted to the hospital to improve cardiac function as much as possible. Vigorous and prolonged therapy was often necessary. The patient was assigned a functional classification according to the criteria of the New York Heart Association when maximum improvement on the medical regimen had been achieved. Sixteen patients were placed in class 2, 64 in class 3, and 12 in class 4. The occurrence of preoperative arterial emboli strengthened the indication for operation in eight class-2 patients.

TABLE 1.—*Mortality in Ninety-two Patients After Mitral Commissurotomy*

Period After Operation, Yr.	Cumulative Mortality No.	%
0-1	12	13
1-2	15	16
2-3	19	21
3-4	21	23
4-5	22	24
5-6	23	25
6-7	26	28

Dr. Ormand C. Julian and his staff performed all operations. The mitral valve was approached through the left atrial appendage in all but a few instances in which an incision in the left atrial wall was required to enter this chamber. Finger fracture of each commissure was then attempted. In some patients a knife was used in order to achieve maximum commissural division.

In each instance, except one where the patient died before the atrium was entered, the surgeon estimated preoperative valve size in millimeters at the widest diameter of the orifice. A similar estimate of postoperative valve size was made in all but 13 patients in whom the surgeon described the opening obtained in terms of percentage widening of each commissure. In order to quantitate the latter information, we have assumed that complete opening of one commissure produces a valve diameter of 25 mm. This assumption is based on the experience of the surgeons at this hospital.

Since operation, all but two surviving patients have been examined periodically by us or by physicians working closely with us in the outpatient clinics. Clinic visits occurred frequently during the first postoperative year and afterward approximately annually.

Two patients were lost to this study two and three years postoperatively respectively. Their state of health is unknown at the time of writing, but information concerning their course as far as it was known has been included in subsequent analyses.

Thirty-nine patients (42% of the entire group) were adequately observed for at least three years after operation. For all patients living after the operation for more than one year, the average period of postoperative clinic observation was 39 months. Of the group alive at the time of writing the median period of observation was 36 months. Eighty surviving patients were observed for one year, 59 for two, 39 for three, 26 for four, and 15 for five years or more.

Postoperative Results

All patients are included in the analysis of results, including four in whom the presence of predominant mitral insufficiency became apparent for the first time at operation. No attempt at valvular repair was made in these persons.

Mortality.—Seven patients (8%) died at operation or during the first postoperative week. All deaths occurred in class-3 patients. Two of these patients died from cardiac arrhythmias during operation, two from postoperative progressive cardiac failure, and one each from hemorrhage from a tear in the left atrial wall, cerebral embolism, and torn posterior papillary muscle with subsequent pulmonary edema.

Nineteen patients died between six weeks and six years after operation (table 1). Eleven of these late deaths resulted from cardiac failure. The cause of death in the remainder is unknown.

Improvement.—All patients were classified according to the amount and duration of postoperative improvement (table 2). Forty-seven per cent of the group had sustained improvement, defined as improvement of one or more functional classes during the first postoperative year, with subsequent maintenance of this improvement during the remainder of the observation period. All patients in this group were observed for at least 18 months.

Twenty-nine per cent of the group had initial improvement, defined as improvement of one or more classes during the first postoperative year, but with deterioration of at least one class during the 18 months to five and one-half years after the operation.

TABLE 2.—*Status of Patients at Least Eighteen Months After Mitral Commissurotomy*

	Patients No.	%
Sustained improvement	43	47
Initial improvement with late deterioration	16	16
Initial improvement with late death	12	13
No improvement		
Alive	7	8
Dead	7	8
Operative deaths	7	8

Factors Affecting Results

Preoperative Functional Class.—The most incapacitated patients before operation were those least likely to have sustained improvement afterward (table 3). Preoperative disability was related closely to the presence of mitral insufficiency, which was more than twice as frequent in class-4 as in class-2 patients.

Atrial Fibrillation.—Fifty-one per cent of the patients had this arrhythmia prior to operation. Six of the seven operative deaths occurred in this group. Sustained improvement took place less frequently in patients with atrial fibrillation than in those with sinus rhythm (table 3). Mitral insufficiency occurred more than twice as often in these persons as in patients with sinus rhythm.

Twelve of 16 patients who had experienced arterial embolization before operation had atrial fibrillation. Postoperative embolic phenomena in patients with atrial fibrillation occurred in the brain in three cases and in the legs in two. In each, the embolism took place in the first month after operation. Three of these patients died. Apart from these instances, no arterial emboli occurred at any time during our observation after commissurotomy.

Of the 45 patients with sinus rhythm before operation, 9 developed transitory postoperative atrial fibrillation reverting to sinus rhythm with or without quinidine therapy by the 10th day after operation. Three patients developed sustained atrial fibrillation.

Mitral Insufficiency.—In 39 patients mitral insufficiency was diagnosed by the presence of a palpable regurgitant jet of blood through the valve at operation. Since hemodynamic and anatomic conditions peculiar to the operation may influence this sign, it is an imperfect diagnostic tool. Nonetheless, it remains the best available.

The regurgitant jet was considered by the surgeon to be mild or moderate in 28 patients and severe in 11. The number of improved persons decreased progressively as the degree of mitral insufficiency increased (table 3). Baker and coworkers [1] also found that mitral insufficiency had an unfavorable influence on operative results.

Occasionally the regurgitant jet was modified by valve fracture. In seven patients mitral insufficiency was produced, having previously been absent. In four of these the resulting regurgitation was mild. This did not appear to affect the patient's prognosis, since three had sustained improvement and the fourth died of a cerebral embolus on the first postoperative day. Three of the seven patients incurred moderate or marked mitral insufficiency at operation. One failed to improve postoperatively and died four months later. The second improved for five years, but then deterioration occurred and he died six years after operation. The third patient was worse after operation but is still alive four years later.

In six patients having a regurgitant jet before valvular manipulation, attempts at fracture increased the amount of mitral insufficiency. None of these patients experienced sustained improvement. Commissurotomy did not decrease an existing regurgitant jet in any patient. In the discussion of the results of operation, the degree of mitral insufficiency in each case is considered as that existing at the beginning of the surgical procedure.

As suggested above, the clinical diagnosis of mitral insufficiency is fraught with error. The presence of a high-pitched apical systolic murmur, louder than grade 2 (grade 6 maximum) and often radiating to the axilla, has been thought helpful in diagnosing this lesion. Only 6 of our 11 patients with severe mitral insufficiency had such a murmur, however. Four patients with severe mitral insufficiency had an apical systolic murmur, grade 1 or 2 in intensity, and one such patient had no systolic murmur at all. Conversely, of 48 patients without a palpable regurgitant jet 18 had a grade 1 or 2 apical systolic murmur and in 4 the murmur was louder than this.

TABLE 3.—*Factors Affecting Postcommissurotomy Results in Ninety-two Patients*

	Duration of Improvement	
	At Least 1 Yr., %	Sustained, %
Functional class*		
2 (16 patients)	81	69
3 (64 patients)	77	44
4 (12 patients)	75	33
Rhythm		
Sinus (45 patients)	90	56
Atrial fibrillation (47 patients)	64	37
Mitral insufficiency†		
None (48 patients)	85	69
Mild or moderate (28 patients)	75	43
Severe (11 patients)	55	18
Cardiothoracic ratio‡		
<60% (39 patients)	91	58
>60% (36 patients)	68	31

* New York Heart Association functional classification.

† In four patients the surgeon did not comment on mitral insufficiency.

‡ Preoperative x-rays not available in 17 patients.

In the absence of hypertension or aortic valve disease, none of our patients with mitral insufficiency had electrocardiographic evidence for left ventricular hypertrophy by the criteria of Sokolow and Lyon.[2] Grant [3] has commented on the lack of autopsy evidence for left ventricular hypertrophy in mitral insufficiency. Wierum and Glenn,[4] however, were able to establish certain combinations of precordial QRS voltages which, in persons with atrial fibrillation, were associated with mitral insufficiency in a large percentage of cases.

Our experience confirms the conclusions of Wierum and Glenn. Seventeen of 24 patients with atrial fibrillation and any degree of mitral insufficiency satisfied their criteria for this lesion. None had hypertension or known aortic valve disease. Use of the criteria of Wierum and Glenn resulted in no false-positive diagnoses of mitral insufficiency.

Careful x-ray and fluoroscopic examination afforded evidence for left ventricular enlargement in only 2 of the 11 patients with severe mitral insufficiency. On the other hand, using these techniques the roentgenologist concluded that the left ventricle was enlarged in six patients with no known lesion stressing the myocardium of this chamber.

Associated Valve Lesions and Hypertension.—The diagnosis of associated significant aortic stenosis was made in two patients. Both had simultaneous aortic and mitral commissurotomy and were initially improved, but only one enjoyed sustained improvement. Four patients were thought to have less severe but definite aortic stenosis because of a typical basal systolic murmur and evidence for left ventricular hypertrophy by electrocardiogram, x-ray, or both. One had sustained improvement after operation, one had only temporary improvement, and two died six weeks and one year after operation respectively.

Table 4.—*Relationship of Preoperative Valve Size to Results*

	Valve Diameter		
Duration of Improvement	<6Mm. (39 Patients), %	6-10 Mm. (41 Patients), %	>10 Mm. (11 Patients), %
At least 1 yr.	91	73	46
Sustained	64	39	18

A characteristic diastolic murmur indicating semilunar valve insufficiency was present after operation in seven patients. In two this was ascribed to pulmonary valve insufficency. Aortic insufficiency was believed to be present in five patients and was thought to be hemodynamically insignificant in four. Only one of these patients derived sustained improvement from mitral valve operation. The two patients who had both mitral and aortic commissurotomy showed postoperative evidence for aortic insufficiency, one having a diastolic blood pressure of 50 mm. Hg and the other 80 mm. Hg.

Serious tricuspid valve disease was not believed present in any patient preoperatively. One patient had essential hypertension with left ventricular enlargement and diastolic blood pressure consistently above 110 mm. Hg. His condition was initially improved after operation but subsequently deteriorated.

Mitral Valve Calcification.—The operator noted severe valve calcification in nine patients, of whom only three derived sustained improvement from the procedure. The remainder were not improved or died. Significant mitral insufficiency was almost a uniform finding in patients with severe valve calcification. It failed to occur only once when the valve was heavily calcified. The surgeon produced an average valve opening 4 mm. smaller in these patients than in those without severe calcification.

On the other hand, mild or moderate calcification did not affect postoperative results. These findings are similar to those in Mounsey's series.[5]

Preoperative Heart Size.—On the whole, patients with large hearts derived less benefit from commissurotomy than did those with smaller hearts (table 3). A high cardiothoracic ratio often indicated the presence of lesions adding to the load of the left ventricle. Less than one-third of our patients without aortic stenosis or mitral insufficiency had cardiothoracic ratios over 60%, but more than two-thirds of those with one or the other of these lesions had a cardiothoracic ratio above this value. Mitral insufficiency was almost three times as frequent in patients with cardiothoracic ratio over 60% as in the other patients in this series.

In most patients with high cardiothoracic ratio without lesions causing stress to the left ventricle, cardiac enlargement can be explained by severe right ventricular hypertrophy secondary to tight mitral stenosis and increased pulmonary vascular resistance. Eleven of 13 patients with cardiothoracic ratio over 60%, but without aortic stenosis or mitral insufficiency, had electrocardiographic evidence of right ventricular hypertrophy and a mitral valve diameter of 8 mm. or less.

Precommissurotomy Valve Size.—As might be expected, the smaller the size of the mitral orifice before commissurotomy the more likely is the patient to experience both initial and sustained improvement after operation (table 4). In patients with the same degree of disability but with different mitral orifice sizes, factors other than mechanical valve obstruction must contribute to incapacity in those patients with the larger valve areas. Mitral insufficiency is certainly one of these factors. All of our patients with preoperative valve diameters greater than 10 mm. had mitral insufficiency. Table 5 clearly indicates the rarity of the coexistence of severe mitral stenosis and severe mitral insufficiency, a conclusion also reached by Gorlin and co-workers.[6] The valve narrowing was likely to be intermediate in degree in patients with mild or moderate mitral insufficiency.

After careful preoperative evaluation, none of our patients was thought to have active rheumatic carditis. It is possible, however, that clinically undetected carditis may in some instances have contributed to disability by causing malfunction of the myocardium itself. At present, no reliable method for evaluation of this type of malfunction exists in patients with valvular heart disease. One might logically suspect, however, that the mitral orifice size would be larger in an individual patient if myocardial incompetence plus mitral stenosis contributed to his disability than if mitral stenosis alone accounted for it. Using this argument, we found

Table 5.—*Relationship of Mitral Insufficiency to Preoperative Valve Size*

	Mitral Insufficiency		
Valve Diameter, Mm.	None, No.	Mild or Moderate, No.	Severe, No.
<6	29	8	0
6-10	20	15	5
>10	0	5	6

no evidence that such myocardial incompetence played a significant role in our patients, since no patient without mitral insufficiency had a mitral valve diameter greater than 10 mm.

Postcommissurotomy Valve Size.—Four of our patients with severe mitral insufficiency had such large valve areas that the surgeon believed it unwise to attempt further opening. None of these patients improved, and two have subsequently died. A fifth patient died of cardiac arrest during induction of anesthesia. In the remaining 87 patients the operator achieved various amounts of widening of the mitral orifice.

When the valve was opened to a diameter of greater than 20 mm., the resulting sustained functional improvement was much more frequent than when lesser amounts of widening were produced (table 6). Our patients usually improved initially regardless of the extent of the commissurotomy, but the benefit to those obtaining only slight relief of their mitral valve narrowing was short-lived.

Five patients, each with initial but temporary functional improvement after operation, underwent repeat commissurotomy three to four and one-half years later. Three of these patients subsequently experienced sustained improvement, one had only temporary improvement, and one did not show improvement and later died. The results of the second procedure are not included in the data presented elsewhere in this communication.

In two of these five patients, the valve diameter discovered at operation was less than that achieved at the previous operation, having decreased by 14 mm. in one and by 17 mm. in the other. In two patients no change in valve size had occurred. In both these patients only a 15-mm. opening had been accomplished at the first operation. The fifth patient was reoperated on elsewhere.

Other Factors.—The patient's age or sex had no influence on the likelihood of improvement after operation. Aschoff bodies, found in the routine left auricular biopsy in 17 patients, likewise did not affect the outlook for benefit from the procedure.

Postoperative Findings

The apical diastolic murmur of mitral stenosis disappeared permanently in eight patients after operation. This appears to indicate a relatively favorable prognosis, since five of these patients had sustained and two temporary improvement and only one derived no improvement from the operation.

In 12 patients apical systolic murmurs present before operation increased in intensity afterward, and in 10 patients an apical systolic murmur was detected after operation for the first time. In only three of these patients did the surgeon believe that mitral insufficiency had increased as a result of the procedure. Appearance or increase in intensity of such a murmur did not adversely affect prognosis, since all but 3 of these 22 patients showed at least temporary improvement after operation.

Apical systolic murmurs decreased in intensity or disappeared in 15 patients after operation. Eight of these had sustained improvement postoperatively, and four improved temporarily. During the period of observation after operation, electrocardiographic evidence for right ventricular hypertrophy by the criteria of Sokolow and Lyon[7] disappeared in six patients and decreased in three. No consistent postoperative changes occurred in direction of the mean frontal plane QRS vector.

Although cardiothoracic ratio usually did not change or decreased slightly during postoperative observation, it increased in 12 patients. Eight of this group had mitral insufficiency, an aortic valve lesion, or hypertension. In four of these eight patients mitral insufficiency was produced or increased as a result of valve fracture. In the remaining 4 of the 12 patients no reason for postoperative increase in cardiothoracic ratio was apparent. Two of these four persons showed improvement despite the increase in heart size.

Table 6.—*Relationship of Postoperative Valve Size to Results**

	Valve Diameter	
Duration of Improvement	<21 Mm. (24 Patients), %	>20 Mm. (63 Patients), %
At least 1 yr.	74	84
Sustained	12	63

* In four patients, each with severe mitral insufficiency, surgeon did not attempt to widen valve.

Comment

In an evaluation of the effect of mitral commissurotomy on the natural history of rheumatic heart disease with mitral stenosis, it is logical to attempt to compare morbidity and mortality of patients operated on to that of similar patients treated medically. Since prognosis relates closely to the patient's incapacity, comparing the data in one patient to those in another requires at least that they receive similar therapy before being assigned a numerical functional classification. Competent medical treatment frequently permits upgrading a patient one or more functional classes. Thus, it would obviously be misleading to compare the prognosis of a completely untreated class-3 patient with that of a patient initially in class 4 but attaining class 3 after intensive therapy.

Unfortunately, the medical literature available to us concerning nonsurgically treated mitral stenosis contains no prognostic report in which the nature of medical therapy throughout the observation period can satisfactorily be ascertained. Olesen,[8] in his large and carefully analyzed series, assigned patients a functional classification on the basis of their symptoms at the time of admission to the hospital. Since it appears likely that previous therapy had varied considerably, one may reasonably assume that the composition of each functional class was heterogeneous. We are thus unable to compare the morbidity or mortality of patients in Olesen's series to that in our patients, who were assigned a functional classification only after a vigorous attempt to achieve maximum benefit from medical treatment.

We encountered these and other difficulties in attempting to compare our patients with those in other groups in the literature. All of Grant's [9] patients, for example, were males. The data of Magida and Streitfeld [10] do not permit establishment of the prognosis of persons in a given functional class.

Efforts to compare our results with those obtained by others in surgically treated patients were somewhat more rewarding, although the outcome in our patients is less encouraging than that described in many reports in the American literature. We believe this discrepancy stems largely from differences in series composition and in methods and time of patient follow-up study, since the amount of valve opening obtained at operation in our series appears to have been comparable to that reported elsewhere.[11]

Bailey and Bolton,[12] for example, do not mention their technique of evaluation after operation. L. B. Ellis and associates [13] reported that nearly all patients maintained their peak postoperative improvement for periods up to six years. Since much of their information about the patient's condition was obtained by questionnaire to the patient himself or from his physician's reports, the possible unreliability of this type of data may account for prognostic differences betwen their series and ours. If contacted by letter, patients and their physicians in our experience are almost uniformly overenthusiastic about the extent of improvement obtained from operation. When closely questioned in the clinic, these patients not infrequently reveal surprising exercise limitation. Perhaps the experience of one life-threatening operation and the fear of requiring another, together with habituation to the symptoms of their chronic disease, permit these patients to develop an uncritical attitude toward their disability.

Some authors may have biased the outcome by eliminating certain operated patients from consideration because of inadequate observation after operation [14] or for uncertain reasons.[15] Similarly, it was difficult to compare our results to those of Maha and Orgain,[16] the majority of whose patients were in functional class 2, or to the findings in the all-male series of Williams and co-workers.[17]

On the other hand, methods in three series in the literature were sufficiently similar to ours to permit critical comparison of results. Baker and associates [1] reported approximately 55% sustained improvement in a group of patients with a median follow-up period for survivors of about 40 months. Forty-seven per cent of our patients had sustained improvement during a comparable time. The incidence of mitral insufficiency was higher in our group than in that of Baker and co-workers.

Turner and Fraser [18] reported sustained improvement in 63% of 250 patients observed for a period of time similar to that of our group. These authors did not include information concerning postoperative valve size or incidence of mitral insufficiency. They probably excluded poor-risk patients from operation more successfully than we, however, since the frequency of atrial fibrillation, valve calcification, and severe cardiac enlargement was distinctly less in their series.

Of a group of 120 patients observed for three and one-half to seven years, F. H. Ellis and associates [19] found 66% with sustained improvement. They did not supply information on the valve opening obtained at operation. The lower incidence of mitral insufficency in their group, half that in ours, may explain some of the discrepancy in results. In addition, follow-up information in one-third of their patients was apparently obtained by letter rather than by personal examination.

All of these authors report that a significant number of initially improved patients had shown deterioration three to four years after operation.

In our patients the two most important factors affecting results were mitral insufficiency and the amount of valve opening obtained at operation. The incidence of sustained postoperative improvement was approximately inversely proportional to the severity of mitral insufficiency. Even mild mitral insufficiency adversely influenced prognosis. If this type of operation continues to be recommended to patients with mitral valve lesions, development of reliable techniques for preoperative assessment of mitral insufficiency should therefore hold high priority in cardiovascular research.

The likelihood of sustained improvement after operation was also closely related to the postoperative valve size. Although most patients benefited temporarily from a minimal widening of the valve, sustained relief of symptoms became far more likely when the surgeon could produce a valve diameter of 21 mm. or more. Baker and associates [1] and Mounsey [5] also observed that improvement tended to be transitory with postoperative valve diameters of less than 20 to 25 mm.

The presence of atrial fibrillation, advanced functional class, severe mitral valve calcification, large preoperative valve size, or significant cardiac enlargement also predicted relatively poor results from operation. All of these factors were closely related to the severity of mitral insufficiency. Adequate fracture of the mitral valve was also less likely in patients with a heavily calcified valve.

It was discouraging that late deterioration followed initial improvement in several patients despite apparently adequate commissurotomy and absence of the adverse prognostic factors noted above. Twenty patients without mitral insufficiency or associated valve lesions obtained a valve diameter of more than 20 mm. at operation and were ranked in functional class 1 a year postoperatively. Two of these patients showed deterioration by at least one functional class and two more died during an observation period ranging from 18 months to seven years and averaging 33 months.

We can only conjecture on the cause of deterioration in this group of patients. Their preoperative heart size, age, and incidence of atrial fibrillation did not distinguish them from patients obtaining more lasting improvement. Gradual restenosis of the valve, myocardial insufficiency, or both may have caused this late deterioration, but available evidence is inadequate to determine its cause with certainty.

The prognosis for patients in a given functional class after operation, without any of the previously noted adverse factors, is thus less good than one might predict for medically treated patients in the same functional class. Patients treated by mitral commissurotomy can be expected to show deterioration more rapidly than the nonsurgical group.

Selection of Patients for Mitral Commissurotomy

In the modern era, when open-heart surgery with the aid of a pump-oxygenator is being evaluated in many centers, one may inquire whether a nonvisual surgical approach still has a place in the treatment of patients with mitral valve disease. Certainly under direct vision more effective plastic repair may be expected. The complexity of cardiac bypass techniques, however, makes it likely that the operative mortality of these procedures in patients with uncomplicated mitral stenosis will exceed that of mitral commissurotomy for some time to come.

Our series indicates that the risk with closed-heart mitral valve surgery is small and that results are excellent provided the procedure is used with discrimination. We suggest that mitral commissurotomy, performed by the technique previously described, be recommended to patients having severe or progressive disability and meeting the following criteria: (1) absence of a high-pitched apical systolic murmur louder than grade 2 in intensity, (2) minimal or no mitral valve calcification seen by fluoroscopy, (3) absence of electrocardiographic evidence for left ventricular hypertrophy by the criteria of Sokolow and Lyon[2] or for mitral insufficiency by the standards of Wierum and Glenn,[4] and (4) cardiothoracic ratio of less than 61%.

Of 75 patients for whom information about these criteria was available, 37 satisfied all criteria. Of these 37, 2 died at operation, 34 (92%) improved initially, and 28 (76%) had sustained improvement after operation. Of the 38 patients failing to meet one or more of these criteria, only 9 (24%) had sustained improvement. It is the latter group whose outlook may improve significantly from application of new techniques in mitral valve surgery.

In view of the high incidence of deterioration in patients deriving an inadequate valve opening from operation, it is obvious that strenuous but skillful efforts to obtain the maximum possible diameter must be made by the operator. The surgeon most experienced in this technique can generally be expected to obtain the best results.

Summary

Ninety-two consecutive patients, subjected to mitral commissurotomy between 1951 and 1957, were repeatedly observed in the outpatient clinic by the same group of physicians. Two patients were lost to the study two and three years postoperatively respectively. The average period of observation after operation for patients surviving more than one year was 39 months. Operative mortality was 8%. Deaths occurring during the several years of observation after operation brought the total mortality to 28%.

Each patient was assigned a functional classification according to the criteria of the New York Heart Association after intensive therapy in the hospital. Although improvement of one or more functional classes occurred for at least one year in 76% of all patients, this improvement was sustained during the remainder of the observation period in only 47% of the total group.

The major factors adversely affecting prognosis were mitral insufficiency and production of an inadequate valve opening at operation. Severe valve calcification made satisfactory commissurotomy less likely and was often associated with significant mitral insufficiency. Mitral insufficiency also occurred frequently with atrial fibrillation, cardiac enlargement, and severe preoperative disability. Although close comparison of the prognosis in our patients with that in nonsurgically treated persons was impossible, it is likely that patients in a given functional class a year after mitral commissurotomy have a less favorable outlook than medically treated patients in the same functional class.

Mitral commissurotomy should be recommended to patients with progressive or severe disability from mitral stenosis if a significant apical systolic murmur, mitral valve calcification, cardiac enlargement, and electrocardiographic evidence for mitral insufficiency are absent. New techniques for mitral valve surgery may offer significant benefit to patients not meeting these criteria.

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COMPARATIVE EFFECTIVENESS OF PHENYLPROPANOLAMINE AND DEXTRO AMPHETAMINE ON WEIGHT REDUCTION

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The anorexigenic effects of phenylpropanolamine and dextro amphetamine were compared in a study of 80 mentally deficient institutionalized patients, without dietary restrictions. One group received dextro amphetamine, two groups received phenylpropanolamine in dosages of 25 and 50 mg. thrice daily, and one group received a placebo. The average changes in weight for the four groups after two weeks were —4.6, —0.9, —0.8, and +0.3 lb. (—2.1, —0.41, —0.36, and +0.14 kg.) respectively. While the dextro amphetamine significantly reduced the voluntary intake of food in the first group, no significant effect was induced by the phenylpropanolamine even in double the recommended dosage.

The problem of weight reduction is receiving widespread attention in view of the demonstrated relationship between longevity and body weight, as well as the more specific relationship between obesity and certain chronic diseases, i. e., diabetes, cardiovascular disease, and arthritis. Probably an equally important motivation for weight reduction, particularly in the female population of certain social strata, is the general acceptance of the leptosomatic configuration as the most attractive and desirable. As a result, considerable efforts are being expended by various organizations primarily to exploit the desire of many to lose weight by the easiest, most rapid, and least painful procedure.

It has been estimated that about 100 million dollars is spent annually for weight-reducing purposes.[1] Unfortunately, it is not generally recognized

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that there may be multiple psychological and physiological factors influencing appetite and that the problem of weight reduction frequently cannot be resolved by a single universally applicable approach. The pharmacotherapeutic approach to weight reduction (as might be anticipated) has received enthusiastic public support, primarily because of the alleged simplicity of treatment, as well as the relative safety and therapeutic effectiveness of the various agents recommended.

There can be no question that certain pharmacological agents [2] (if prescribed by physicians who comprehend the complexities of the problem of weight reduction) may be effective adjuncts in a total therapeutic regimen (diet and psychotherapy). On the other hand, without sufficient scientific evidence to support claims of specific anorexigenic properties,[1] pharmaceuticals are being made available to the public without prescription. The present study was conducted to compare the clinical effectiveness of one of these agents (phenylpropanolamine) with a related sympathomimetic amine of proved therapeutic value (dextro amphetamine). Although phenylpropanolamine is currently widely exploited as the principal or the allegedly therapeutically effective chemical ingredient of several widely advertised "no-diet" reducing nostrums, satisfactory evidence does not appear available at this time to support the claimed mechanism of action. Evidence for therapeutic efficacy is based in part on clinical observations attesting to the value of the above compound as an effective agent in controlling appetite and in the reduction of weight of obese subjects. The majority of the subjects studied, however, in addition to receiving phenylpropanolamine were placed on a low-calorie diet. Subsequent experience has proved the drug to have either questionable or no value as an anorexigenic agent.[1]

Method

To obviate some of the psychological factors influencing any weight-reduction program in the mentally alert population, institutionalized obese patients with idiopathic mental deficiency were selected for the present study. These otherwise physically normal subjects had been residents of the institution for a number of years, and their body weight had been recorded monthly since their admission. There had never been any dietary restriction either before or during the study, and their daily food intake consisted of a well-balanced diet known to contain about 3,000 calories—an intake, in view of their obesity, obviously well above their energy requirements.

Despite the low intellectual capacity of the subjects, the study was nevertheless conducted with use of the "blind" procedure, so that none of the personnel associated with the project were aware of the nature or identity of the drugs administered. The drugs were compounded and labeled by an independent pharmacist and their compositions made known to us only after completion of the study.

The 81 subjects selected for the study were divided into four approximately equal groups, and each subject of each group was given one of the four preparations under investigation three times a day, one hour before meals, for a period of six weeks. The drugs were administered by cottage supervisors (not aware of the identity of the drugs) who made certain of their ingestion by the subjects and were responsible for recording the weekly weights of all cottage residents participating in the investigation.

Table 1.—*Weight Changes with Phenylpropanolamine Hydrochloride, Twenty-five Milligrams Three Times a Day*

Subject	I.Q.	Age, Yr.	Sex	Height, In.	Initial Weight, Lb.	Weight Change/ 2-Wk. Period, Lb.			Total Weight Change, Lb.
						2	4	6	
1	44	67	F	62.0	175.5	−0.5	−3.0	−1.0	−4.5
2	38	20	F	62.5	136.2	−0.2	−2.0	+1.0	−1.2
3	25	54	F	66.0	162.0	−2.0	+2.0	−2.0	−2.0
4	30	24	F	66.0	176.0	+2.0	−2.0	+4.8	+4.8
5	46	39	F	68.5	160.5	−2.3	−1.7	+1.5	−2.5
6	41	35	F	68.0	189.0	−2.0	+3.0	−2.0	+3.0
7	31	40	F	61.0	163.2	−2.7	−0.5	+5.5	+2.3
8	15	40	F	51.2	137.0	−1.2	*	*	−2.2
9	28	28	F	57.0	131.0	+0.2	*	*	−2.0
10	29	45	F	65.0	217.0	+0.2	*	*	−1.0
11	43	15	F	61.5	151.2	−2.2	+0.8	−5.0	−6.4
12	21	11	F	51.0	86.0	+0.5	−2.0	−1.5	−3.0
13	Idiot	19	M	68.5	168.5	+5.3	−3.8	+2.0	+3.5
14	27	43	F	66.0	181.5	+2.3	+7.7	+1.5	+11.5
15	43	21	M	64.5	174.2	−2.2	0	−1.0	−3.2
16	33	45	M	66.0	182.0	0	−3.0	+3.0	0
17	59	17	M	65.0	184.0	−7.0	−4.0	+1.0	−10.0
18	22	27	M	67.5	220.0	−4.0	−5.0	+4.5	−4.5
19	20	36	M	61.5	186.0	−2.0	+2.0	+1.0	+1.0
Mean values	33	33		62.8	167.4	−0.9	−0.6†	+0.7†	−0.9

* Weights not recorded.
† Mean of recorded values.

Only after completion of the study was it disclosed that in one group of 19 subjects each had received 25 mg. of phenylpropanolamine three times a day and in another group of 19 each was given 50 mg. of the drug three times a day. In a third group, comprising 22 patients, each received 5 mg. of dextro amphetamine. The fourth group, consisting of 21 obese subjects, received before meals a placebo with physical characteristics indistinguishable from those of other capsules under investigation.

Results

Table 1 presents the results obtained in 19 subjects before and during the administration of 25 mg. of phenylpropanolamine three times a day. In 13 of the subjects there was either no change in weight or a weight loss which varied from 1 to 10 lb. after six weeks of study. In 6 of the subjects there was a gain in weight of 1.0 to 11.5 lb. during the period of investigation. The average weight loss was 0.14 lb. per person per week and 0.86 lb. per person after six weeks' use of the drug.

Table 2 presents the findings for the 18 subjects receiving 50 mg. of phenylpropanolamine three times a day for six weeks. Use of the drug was discontinued in one additional subject after two weeks because of an illness not related to drug ingestion. Of the 18 subjects completing the study, 12 showed no change in weight or a weight loss of 1 to 6.0 lb., and in the remaining 6 subjects there was a weight gain of 1 to 7.0 lb. The average weight loss per person per week was 0.13 lb., and for the six weeks it was 0.76 lb.

Table 2.—*Weight Changes with Phenylpropanolamine Hydrochloride, Fifty Milligrams Three Times a Day*

Subject	I.Q.	Age, Yr.	Sex	Height, In.	Initial Weight, Lb.	Weight Change/ 2-Wk. Period, Lb.			Total Weight Change, Lb.
						2	4	6	
1	40	46	F	57.0	147.0	—1.0	—4.5	0	—5.5
2	34	46	F	61.0	162.0	—1.8	+4.5	—1.7	+1.0
3	22	40	F	60.0	148.0	+0.2	—1.2	0	—1.0
4	37	39	F	68.0	167.0	—1.0	+2.0	0	+1.0
5	62	43	F	63.0	174.0	+6.2	0	+0.8	+7.0
6	64	15	F	64.0	159.5	—1.5	—0.8	—0.2	—2.5
7	20	48	F	56.8	203.5	+1.7	*	*	+1.7
8	17	18	F	63.5	147.8	—2.0	*	*	—2.0
9	15	48	F	58.0	198.2	+3.0	*	*	+5.6
10	33	15	M	60.0	137.0	+4.8	—2.3	+2.3	+4.8
11	60	36	M	72.0	234.0	—1.5	+0.5	+1.0	0
12	Idiot	8	M	49.0	67.0	—6.5	+1.5	+1.0	—4.0
13	11	20	M	57.5	119.0	—1.8	+2.8	—2.5	—1.5
14	57	42	M	62.0	175.0	+1.8	—3.8	+0.5	—1.5
15	49	24	M	55.2	171.5	—7.3	+1.6	+3.0	—2.7
16	39	28	M	70.0	220.5	—7.0	0	+1.0	—6.0
17	40	38	M	67.0	252.5	—6.0	+2.0	+1.0	—3.0
18	20	31	M	65.0	195.0	—8.0	0	+3.0	—5.0
Mean values									
	34	32		61.6	170.9	—1.5	+0.1†	+0.5†	—0.8

* Weights not recorded.
† Mean of recorded values.

The changes in weight recorded for the 21 subjects given 5 mg. of dextro amphetamine three times a day are presented in table 3. Here again use of the drug was discontinued in one additional subject after two weeks. In the 21 remaining subjects, 19 lost from 0.2 to 10 lb. and 2 showed a weight gain of 2.3 and 3.0 lb. during the six weeks of the study. The average weight loss per person per week was 0.76 lb., and for the six-week period it was 4.56 lb.

Table 4 presents the results on 21 subjects who received a placebo three times a day for a period of six weeks. Eight of the subjects experienced a weight loss of 0.2 to 9.5 lb., and the remaining 13 subjects showed a gain of 0.3 to 6 lb. for the six-week period. There was an average weight gain of 0.05 lb. per person per week and 0.3 lb. per person during the entire period of the study.

It is apparent from the data that the changes in weight resulting from the administration of 25 and Administ phenylpropanolamine three times a day were no more significant than that associated with the administration of the placebo. On the other hand, the mean weight loss of 4.56 lb. per person resulting from the ingestion of dextro amphetamine for the six weeks of the study is statistically significant and in conformity with findings of numerous previous studies. The fact that not all of the subjects receiving dextro amphetamine demonstrated a significant weight loss (some even showed a weight gain) perhaps serves to emphasize further the existence of multiple variables influencing weight reduction in the present group of subjects with low intelligence quotients. Thus, the therapeutic effectiveness of a recognized pharmacologically potent anorexigenic agent may, even in mentally deficient subjects, be neutralized, possibly by cortical or subcortical influences.

Comment

The results demonstrate that two closely related sympathomimetic amines, when studied under similar conditions with use of the "blind" procedure, possess significant differences in anorexigenic potency. Phenylpropanolamine, when administered in recommended doses, and even in twice the supposedly therapeutic doses, failed to effect a statistically significant reduction in weight. The changes in weight associated with the ingestion of phenylpropanolamine were of approximately the same magnitude as those accompanying the ingestion of

Table 3.—*Weight Changes with Dextro Amphetamine, Five Milligrams Three Times a Day*

Subject	I.Q.	Age, Yr.	Sex	Height, In.	Initial Weight, Lb.	Weight Change/ 2-Wk. Period, Lb.			Total Weight Change, Lb.
						2	4	6	
1	65	19	F	66.5	168.0	—8.5	+0.7	—2.2	—10.0
2	67	57	F	61.0	166.0	—1.8	—2.2	—1.0	—5.0
3	71	45	F	63.0	198.2	—1.2	—4.3	+0.8	—4.7
4	20	45	F	48.0	152.0	—1.3	—4.7	+1.5	—4.5
5	53	58	F	63.0	138.0	—1.8	—3.7	—4.5	—10.0
6	65	14	F	65.0	200.5	—8.5	0	—1.5	—10.0
7	52	46	F	58.0	143.2	—2.7	+1.7	—3.2	—4.2
8	40	34	F	63.0	144.5	—2.0	+1.0	—3.0	—4.0
9	14	48	F	56.0	163.8	—2.8	*	*	—4.6
10	21	61	F	57.0	156.2	+4.3	*	*	+2.3
11	25	27	F	56.8	182.2	—1.0	*	*	—3.4
12	25	40	F	61.0	148.2	+1.0	*	*	—3.2
13	76	27	M	57.0	229.5	—6.5	+2.0	0	—4.5
14	46	26	F	62.0	121.2	—1.0	—7.2	—0.8	—9.0
15	33	14	M	61.5	125.5	+1.0	0	—1.3	—0.3
16	Imbecile	13	M	59.0	111.0	—4.0	—2.0	—3.0	—9.0
17	Undetermined	21	M	72.5	205.0	—1.5	+2.5	—1.2	—0.2
18	19	39	M	61.5	162.5	—1.0	—1.5	0	—2.5
19	36	51	M	67.0	222.0	0	+2.0	+1.0	+3.0
20	Undetermined	20	M	66.0	150.0	—7.0	—3.0	0	—10.0
21	27	42	M	58.0	145.0	0	—6.0	+4.0	—2.0
Mean values									
	42	36		61.1	163.5	—2.2	—1.2†	—0.7†	—4.6

* Weights not recorded.
† Mean of recorded values.

a placebo. The administration of dextro amphetamine, on the other hand, was associated with a statistically significant reduction of weight.

There is considerable experimental evidence to indicate that certain sympathomimetic amines, particularly amphetamine and dextro amphetamine, can facilitate weight loss in both animals and man.[3] The weight loss apparently results primarily from a reduction in food intake due to a diminution of appetite. Although the exact mechanism of action is unknown, a direct central nervous system effect is postulated, since denervation of the alimentary tract in dogs does not alter the anorectic potency of the drugs effective in intact animals. Phenylpropanolamine, also a sympathomimetic amine, has pharmacological properties presumably most similar to those of ephedrine. The stimulating effects of ephedrine and phenylpropanolamine on the central nervous system are believed to be less intense than that of amphetamine.

TABLE 4.—*Weight Changes with Placebo, Three Times a Day*

Subject	I.Q.	Age, Yr.	Sex	Height, In.	Initial Weight, Lb.	Weight Change/ 2-Wk. Period, Lb.			Total Weight Change, Lb.
						2	4	6	
1	57	48	F	66.5	163.0	—6.0	—0.8	—2.7	—9.5
2	43	26	F	61.0	171.8	+1.2	0	—2.0	—0.8
3	42	39	F	66.0	171.0	+1.0	+1.0	+2.0	+4.0
4	49	54	F	59.0	144.0	0	—4.0	+3.0	—1.0
5	48	30	F	62.0	136.0	—4.0	+6.0	—7.0	—5.0
6	30	32	F	53.0	137.0	0	+2.0	0	+2.0
7	66	43	F	59.5	130.8	+1.9	—1.2	0	+0.7
8	10	52	F	62.5	191.8	+1.0	*	*	+0.7
9	22	55	F	61.5	180.2	+0.6	*	*	—0.2
10	32	17	F	52.2	119.2	+2.0	*	*	+0.8
11	16	40	F	60.5	161.0	+1.5	*	*	+4.5
12	23	43	F	58.5	177.2	+2.3	*	*	+1.8
13	70	61	M	65.0	201.0	+1.0	+1.0	0	+2.0
14	44	16	F	56.0	106.0	0	+3.0	—1.0	+2.0
15	25	19	M	60.0	125.2	+0.3	—1.0	+1.0	+0.3
16	Undetermined	17	M	57.0	85.0	+3.0	—4.5	+0.5	—1.0
17	30	18	M	67.5	171.8	—0.8	—2.0	—1.0	—3.8
18	30	30	M	69.0	173.8	0	+1.7	+0.5	+2.2
19	31	26	M	65.0	200.0	+1.0	0	+5.0	+6.0
20	16	28	M	65.0	168.0	—3.0	—1.0	+1.0	—3.0
21	45	44	M	67.0	187.0	0	+3.0	0	+3.0
Mean values	37	35		61.6	157.6	+0.1	+0.2†	0†	+0.3

* Weights not recorded.
† Mean of recorded values.

The results of the present investigation lend support to the concept that phenylpropanolamine does not exert a marked central nervous system effect, at least insofar as appetite reduction is concerned, and indicate that it is of little therapeutic value as a pharmacotherapeutic adjunct in the management of obesity. In view of the generally recognized effectiveness of psychological forces alone on appetite control, these results do not preclude the possibility of weight loss in a receptive or susceptible population when phenylpropanolamine, or even a placebo, is administered along with sufficient psychological motivation provided by a physician. There thus appears to be little justification or rationale for the promiscuous use of pharmacological agents whose therapeutic effectiveness cannot be proved or justified.

Finally, in view of the many psychological and physiological factors involved, as well as the recognized increased incidence of certain disease entities in the obese population, weight reduction should be supervised by physicians, particularly when drugs are used as therapeutic adjuncts.

Summary and Conclusions

The comparative anorexigenic potencies of phenylpropanolamine and dextro amphetamine were determined in a quadruple-blind study conducted on 81 obese mentally deficient subjects. There was no attempt to restrict food intake, and the known caloric consumption was at least 3,000 calories per day. These subjects were selected to obviate insofar as possible the many psychological factors known to influence weight reduction in the mentally alert population. The results failed to demonstrate a significant reduction in weight in the groups of subjects receiving 25 and 50 mg. of phenylpropanolamine three times a day and those given a physically indistinguishable placebo. In the group of subjects receiving 5 mg. of dextro amphetamine three times a day over a similar period of time, there was a statistically significant reduction of weight. Although related chemically to dextro amphetamine and retaining certain of its peripheral properties, phenylpropanolamine, as indicated by this study, differs in that it does not possess significant anorexigenic potency.

19th Street and Massachusetts Avenue S. E. (3) (Dr. Fazekas).

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The drugs for this study were compounded and labeled by Charles J. KoKoski, Ph.D., assistant professor of pharmacy, School of Pharmacy, George Washington University, Washington, D. C.

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PANEL DISCUSSION ON PSYCHIATRIC EMERGENCIES IN GENERAL PRACTICE

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A GENERAL PRACTITIONER'S EXPERIENCE

Richard H. Gwartney

In psychiatric emergencies either the patient or his family will generally demand immediate action. This pressure on the physician probably results in more mistakes than any other single factor. The state of acute anxiety or panic is unbearable, but sedatives or tranquilizers provide merely temporary relief. The better the patient's personal life is known to the physician, the more intelligently can the crisis be handled. Kindness and understanding shown by the physician will calm even highly disturbed patients in most instances. When there is evident danger of suicide, the patient should be hospitalized by persuasion or by commitment, if necessary. The psychiatrists in the community should be considered a resource to be called on when an emergency demands more psychiatric skill than the physician himself possesses. But the physician should not be hasty with either sedation or hospitalization, for they are seldom necessary when the patient's problem is recognized and the solution is offered.

Undoubtedly anxiety would head the list of psychiatric emergencies encountered by any physician regardless of specialty, for to a lesser or greater degree this reaction is found in almost every patient with whom he is confronted. We too seldom take into consideration what we may symbolically represent to the patient and, unless his anxiety is acutely manifested, are too glibly taken in by his recital of physical symptoms which are often masks for chronic anxiety. In such cases it may come as a surprise that removal of one of these "useful symptoms" precipitates a severe anxiety state. The state of acute anxiety or panic is unbearable, and certainly some immediate measure for relief must be instituted. However, if barbiturates or tranquilizers are given, it behooves the physician to point out that these provide merely temporary relief at best and that what is needed is psychotherapy, whether it be formal or informal. The family physician can go a long way by merely "listening these patients out."

Specific Problems

What physician has not been called on to attend a patient with a reactive depression which obviously has just had its onset in the death of a close one, injury, illness, or personal catastrophe? Here the wise physician will be aware that a person must endure a certain amount of grief for his future mental health and thus he will not be pressured into too quickly dispelling it—or should I say depriving the patient of it—by some medicinal means.

Amid the many and varied costs of industrial and scientific progress, at least two of psychiatric significance should be pertinent to this discussion. First, mechanization predisposes to injuries, and, although skillful surgical treatment is given, the emotional impact of the loss of an eye or a limb or a head injury is often ignored or minimized. I have frequently seen such an attitude on the part of a physician contribute to the prolongation of physical symptoms and emotional manifestations which eventually demand more attention and cause more disability than the original trauma.

The second cost is illustrated by the following incident: The distraught daughter-in-law of a particularly obstinate, despotic, senescent woman shook an accusing finger at me, saying: "You doctors are going to be sorry that you have kept all of these old people alive." Dramatically she had stated the problem of geriatrics confronting the general practitioner, who must often attend the disoriented, noisy, confused, aging patient whose mental symptoms have been either sudden or incipient in their onset but are now of violent nature.

The shortage of beds for such patients in mental hospitals precludes commitment, while private resources are expensive. However, in my experience many of these aged persons actually do much better when they can be cared for at home with the aid of a well-tolerated tranquilizer, a realistic, affectionate, close relative, and an empathic physician with an untiring ear.

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Depressions, so frequently disguised with physical symptoms, become of necessity a psychiatric emergency if suicide is to be prevented in many of these cases. Depressions, especially those of a psychotic nature, are best treated by a qualified psychiatrist but should be diagnosed early by the family physician. It is essential that the physician makes an effort to determine the depth of depression by questioning—leading out with questions which may be graded upward as to "How are your spirits? Are you blue? Does life seem worth living? Do you get any morbid ideas? Tell me about them."

A valid warning worth repeating here is that the patient who appears to be recovering from a depression is far more apt to be a candidate for suicide than one who is deeply depressed. When the physician becomes suspicious of suicidal inclinations in a patient, it is his duty to inform the family and to make certain that some reliable person is with the patient at all times, preferably in a hospital, until the patient can be seen by a psychiatrist.

Delirious states, whether induced by chemicals, such as bromides or barbiturates, or by metabolic disorders, such as in fever or heart failure, are quite frightening to both the family and the physician. Strecker and Ebaugh note that while toxic psychosis is found in only about 10% of patients admitted to psychiatric clinics it is the most common major mental disorder treated by the general practitioner. One of the earliest symptoms is the fluctuation in consciousness from a state of complete confusion to one of clearness. Later, delusions and hallucinations appear. Obviously, the first consideration of treatment must be prevention of further poisoning. Determination of the source—exogenous or endogenous—is primary, and then the source is corrected or treated specifically.

Alcoholism, both chronic and acute, may frequently be encountered by the general practitioner and should be treated according to the stage of the disease and the physical and mental state of the patient. In the acute exacerbation, such drugs as apomorphine are to be avoided and the promazine drugs may cause more liver dysfunction. In my opinion, the safest drug for a patient in the acute state is probably still paraldehyde. The proper attitude of the family physician may encourage an alcoholic, who is usually poorly motivated, to seek psychotherapy or at least to attempt some rehabilitative measures.

The emotional problems of pregnancy are manifested in some of the complications of the first trimester, such as hyperemesis and threatened abortion, later toxemias, and, of course, the development of postpartum psychosis. In the earlier phases of their onset, the emotional component of these symptoms may be rewardingly treated by the general practitioner. He is in an ideal position to dispel his patient's anxiety.

The dangerous patient is seen in the epileptic furor and aggressive psychopathic states often induced by alcohol or drugs, in the schizophrenic process, in the manic-depressive psychoses, and in the various paranoid states. Here therapy by the physician may be interpreted by the patient as an attack and withdrawal from the case as rejection; thus the doctor becomes the object of his hostility. Needless to say, early detection of these cases is essential, with referral to a qualified psychiatrist or to the state hospital.

The less obvious psychological emergencies may go unrecognized by both family and physician and are evaluated as such only in retrospect, when their impact has already done its damage. These include the many crises in life, such as marriage, pregnancy, illness or injury, loss of a close one, and threat of financial or personal disaster. It is undoubtedly in this field that the family physician can make his greatest contribution through knowing his patient totally and, thus, to anticipating (but not suggesting), inquiring into, and recognizing these crises and providing, if possible, some sort of shock absorber through his mature empathy and insight. In such a role the physician would serve ideally in a preventive capacity.

Attitude of the Physician

Unfortunately, however, far too often the physician is called in the psychiatric emergency to see a stranger who, prodded by his panicky family, demands immediate and permanent relief in one treatment. The strength of these demands rings loudly through the physician's own emotional conflicts and echoes in his orientation to physiological medicine. While the first requirement in such chaos is to determine which one is really the patient, the physician too frequently is stampeded into doing what he rationalizes as "the humanitarian thing."

The attitude of the general practitioner is the most important factor in the original contact and often spells the difference between success or failure in handling the situation. Essential features of this attitude include calmness, confidence, empathy, and, if need be, authoritative firmness. It may be necessary to administer psychiatric first aid to the family before seeing the patient, even as one might require hoists and a jack to remove a truck from an injured driver's leg. I have found that often this requires no more than the calming effect of a consistently unhurried, unharried approach to the problem, forestalling the crisis which seems imminent in both patient and family. All too frequently the unwary physician is pressured by the projected tensions of the family and his own emotional insecurity to "do something—just anything—but do it right now." Unfortunately this is often done to the detriment of the doctor's best medical judgment and of his prestige when and where both are badly needed. Equanimity, a necessity in all emergencies, is an absolute essential in psychological emergencies, and large doses of it produce remarkable results in the fearful family, if not also in the patient, permitting the physician to avail himself of his best psychological judgment in a particular case.

While a background of medical knowledge is essenital to the recognition of various psychological emergencies, the result of training and experience is the greatest teacher. In such experiences, the honest physician will begin to recognize both personal and professional assets and liabilities and, becoming aware of deficiencies in both areas, he will seek guidance and assistance from competent sources. If the general practitioner lends himself to the indiscriminate prescribing of tranquilizers, with no effort to determine and eliminate underlying emotional causes, I predict that more "iatrogenic psychiatric emergencies" will arise to plague him or some other physician.

UNDERSTANDING THE MEANING OF PSYCHIATRIC EMERGENCIES

Alfred Auerback

Each day medical practice brings its crises and emergencies, both medical and psychiatric. The crises of everyday life—bereavement, financial stress, problems of school or work, marital strife, disappointments in love, or sexual maladjustment—lead many people to turn to the family doctor for help, advice, and guidance. Repeatedly he is required to be the comfort, confidant, or pillar of strength to the person or family seeking his assistance.

Acute anxiety attacks, panic reactions, hysterical outbursts, and acute psychotic episodes are accentuations of the same problems, though all the reasons for their appearance are usually not apparent. The same kindness and understanding shown by the physician will calm even highly disturbed patients in most instances. The better the patient's personal life is known, the more intelligently can the crisis be handled, often without need for sedation or hospitalization. While psychiatric consultation may be sought, usually the physician will handle the emergency himself.

Basis for Symptoms

It must be realized that there is a logical basis for every mental or emotional symptom that appears, no matter how irrational it seems. The more we understand the patient's inner life, the better we are equipped to handle the crisis he presents. For this reason the urge to "do something" that tempts the physician must be pushed to the background while he tries to understand what is happening within the disturbed person. Frequently just letting the patient talk will reveal a great deal about what is going on.

For example, a woman celebrating her wedding anniversary developed what she thought was "heart trouble" and required emergency treatment. Her heart trouble was of a different nature. Her husband had just told her how happy he was in their marriage, when the wife knew he was repeatedly unfaithful. Unable to confront him with the truth, she developed an acute anxiety attack. In another instance, a professional man awoke one morning very agitated for no apparent reason. On careful questioning he remembered thinking of his approaching 50th birthday and then suddenly recalling a bit of childhood misinformation that a man's sexual life ended at the age of 50. Immediately after this thought his anxiety attack had appeared. Recently a 40-year-old woman decided to resume her schooling after a 20-year interval during which she had raised her family. Within a few weeks she found herself unable to study and becoming depressed. After a series of psychiatric interviews she became aware of having a physical attraction to her teacher and she was afraid of becoming promiscuous. She connected this with similar fears of promiscuity which occurred when she was a teenager in high school and which had led to an impulsive and unsatisfactory marriage.

Too often a patient comes to his physician somewhat upset or tearful, demanding, complaining, or uncooperative, and the physician is apt to react with annoyance, anger, or anxiety. These may be the prodromata of serious trouble, but if this fact is not understood the physician may miss these appeals for help. A parent may bring in a son or daughter or a husband may bring his wife and ask for aid, describing their behavior as depressed, anxious, or bizarre. However, when the patient is interviewed, he or she summons all his resources to put on a good appearance and give every indication of being normal. In view of this the patient is dismissed and the family told that all is well or that "he is just a little nervous." At times the physician may scold or reprimand the patient or say that he is malingering and his complaints should be ignored. Obviously, this only increases the mental turmoil for patient and family and such a physician misses the warning signals.

Everyone has his own private worries and problems. At times everyone feels the need for someone to talk to, for some place to share or shake these worries. The overly conscientious person, reflecting a strict upbringing, has his load of guilts which may crop up and threaten to overwhelm him. Religion provides comfort for those who seek its help. Many persons turn to their personal physician to talk out their hates, guilts, sins, and needs. They look on him as an understanding parental figure. The accepting, nonmoralizing physician can provide inestimable help for his patients. The more he can encourage his patients to confide in him, the better are the therapeutic results. In most cases the physician does more good by merely listening with a noncritical attitude than by trying to actually solve the problem or give advice. To use a hackneyed phrase, keep your ears open and your mouth shut.

Problems of Management

The physician will be called in, often at night, to see an extremely anxious or panicky patient. He may show hyperventilation and every evidence of uncontrolled excitement. The patient turns to the physician for help and reassurance, and it is essential that the physician not become anxious or feel overwhelmed himself. By being calm and reassuring in both word and action, he can nearly always quiet the patient's agitation or distress. The physician should permit the patient to talk about himself and, in addition, should obtain all possible information from the family or friends. Too often the physician feels the need for action and may give sedation by injection or hospitalize the patient when such actions are not indicated. A quick examination to rule out an organic process will provide assurance that no grave disorder, such as a heart attack, stroke, or other cataclysmic disease, has befallen him. Many require no medication, but sometimes a pill, whether aspirin or mild sedative, will have an almost magical effect; at other times an injection of a barbiturate or scopolamine compound may be needed. It is rarely necessary to put the anxious, frightened patient in the hospital, and a reassuring discussion with him and his family may suffice to handle the crisis.

However, when the panic is a manifestation of an acute psychotic process, such as beginning schizophrenia or manic excitement, acute intoxication due to alcohol, barbiturate, or bromides, or some such preexisting organic process as brain disease or heart failure, the management must be different. The acute psychotic behavior characterized by confusion and disorientation and often associated with auditory or visual hallucinations may be quieted with a reassuring approach, but frequently the patient is unresponsive. The administration of a medicament, particularly by injection, may be interpreted by a confused, disoriented person as an attack on him and may precipitate assault. Such patients should be placed in a hospital equipped to handle their condition, one where the patient is protected from impulsive behavior which might be injurious to himself or to others. It must be realized that such a person may respond to his auditory hallucinations by attempts at self-injury, self-mutilation, suicide, or, rarely, homicide. Frequently the patient quiets markedly once he is in hospital and realizes he runs no risk of injury to himself or others. His hospital management requires the specialized care of a psychiatrist who will study the case and ascertain the treatment best suited for the patient. Every physician should know where the acutely disturbed patient may be hospitalized in his community and the process whereby this can be done. Often he is too ill to cooperate, and commitment procedures are necessary. If the physician is acquainted with these regulations beforehand much time can be saved and confusion avoided.

A suicide attempt by a patient, particularly if successful, is very disturbing to the attending physician. In most cases the suicide victim seeks medical help in the period immediately preceding his attempt. In San Francisco a study by Motto and Greene was made of 175 successive cases of suicide and 197 hospital admissions for suicide attempts, a total of 372 cases. The majority of these persons were under medical attention in the month or so preceding the suicide try. In 14 cases the suicide attempt occurred the same day the person saw the physician, some immediately on leaving his office. One-third of the suicide attempts were by the use of barbiturates medically prescribed.

It would be a tremendous boon to us as physicians if we had clear-cut indicators pointing out the potential suicide. Unfortunately there are no definite ways of detecting this in a person. Shneidman and Farberow have demonstrated that in 75% of the suicide cases they studied in Los Angeles the person involved had previously threatened or attempted to take his life. They felt that suicidal behavior, whether attempted or threatened, must be taken seriously inasmuch as the next suicidal gesture may be the final one. Whenever a patient talks of suicide the physician should give some thought to the possibility. Too often he will not voice the idea, and the physician, though suspecting its presence, hesitates to ask, mistakenly believing that mentioning the word will trigger the act. On the contrary, most patients welcome the chance to talk out their fears and disappointments and will discuss suicidal preoccupations.

Ordinarily, the neurotic patient does not attempt suicide other than in cases of hysteria. The neurotic may make an attempt more to attract attention or to punish someone else but usually does not plan to go through with the deed. However, in threatening to jump out the window or off the bridge, he may accidentally lose his balance. The fact that sleeping tablets or other poisons have been ingested may not be reported soon enough for their effective removal, or no one may hear the car motor running in the garage although the patient expected to be found in time. Consequently, any emotionally disturbed person who threatens suicide, even if it seems jokingly, should have a psychiatric evaluation to determine the suicide risk. Unless a physician knows his patient extremely well he carries a heavy responsibility in making this evaluation himself.

The physician wishing to recognize the potentially suicidal person does have some diagnostic criteria. Every depressive reaction or mention of suicide should be given consideration. If the patient has a history of a previous suicide attempt, the likelihood of a repetition is great. When he is extremely agitated, is apathetic and disinterested in his family or personal activities, or has profound feelings of guilt, unworthiness, and need for punishment, the risk is high. In all these cases the patient should be hospitalized, by personal or family persuasion, if possible, or by forcible measures, such as commitment, if necessary.

Many medical disorders, including heart disease, diabetes, and thyroid dysfunction, may be accompanied by mental confusion, disorientation, and impulsive behavior. These toxic reactions require primarily medical management, and correction of the physical disorder will in most instances clear the patient's mental confusion. Sometimes when a person is informed he has heart disease or cancer or that a surgical procedure is necessary he reacts by becoming extremely anxious, agitated, or even depressed to the extent of suicide.

Summary

Many people turn to the family physician as an understanding paternal figure during periods of stress in their lives, and they are helped when they are permitted to "talk out" their troubles. Even in most emotional and some mental emergencies the patient is benefited by a similar "talking out" of his fears. The physician who understands their needs can provide tremendous help for these persons without use of medication or hospitalization. In emergencies due to psychotic reactions or acute intoxications, hospitalization is essential and psychiatric consultation indicated. Many suicidal attempts occur in persons under medical care. Physicians can learn the warning signals for the potential suicide and can help such a person by prompt hospitalization and/or psychiatric care.

THE MANAGEMENT OF PSYCHIATRIC EMERGENCIES

Sam Nelken

In any emergency a physician has to meet, his task is, first, to size up the situation and, second, to minimize the threatened harm. Occasionally, one might have a chance to help another capture a fleeting opportunity rather than ward off harm, but I will restrict the present discussion to the emergency of danger.

Recognition of the Situation

Sizing-up begins with recognizing that there is an emergency, that an unforeseen situation which demands prompt intervention has suddenly appeared. In psychiatric emergencies, the patient's disturbance is so moving to others that anyone who notices him will recognize there is something much amiss, unless the observer is abnormally insensitive to other people. When physicians overlook psychiatric emergencies, it is often because they are so preoccupied with the idea of organic disease that they fail to consider the psychiatric component.

Following are a few samples of recognizable psychiatric emergency. Perhaps you have gone out at night to see a man sitting up, breathing hard, fearing he is about to die, and clutching at a heart which sounds overactive but otherwise normal. Perhaps a primipara has been unable to sleep after delivery, has ignored her baby, has refused food, has wept a little, has hardly spoken, and could not explain her depression. In your office, a man has complained of indefinite aches and insomnia, has been unable to keep his mind on giving his history, and has seemed tense, restless, gloomy, and discouraged. Or a family calls you to deal with a young man who has locked himself in his room and shouts through the door that he knows they are trying to electrocute him. In each such case, there is acute suffering to be relieved and other impending damage, from suicide or homicide on down the scale, to be averted. In most cases, there will be an acute psychiatric disorder still needing treatment when the emergency proper is past, and the handling of the emergency should, if possible, lead smoothly into such treatment, which may be conducted by the general practitioner if he knows how or by a psychiatrist when that seems better.

In emergencies—true emergencies—there is no time for deliberate and cautious evaluation but, if intervention is to be helpful, the physician must act from some conception of the structure of the situation and of the process to which it belongs. Life presents many personal emergencies; for instance, a mother may take a child to the beach and lose the child in the surf. If you are not a psychiatrist or any sort of physician, you may still easily understand her panic and grief and have some idea how to help. Psychiatric emergencies are a kind of personal emergency, set apart from others mainly by being hard to understand; we can easily see why a woman is grief-stricken at losing a child but not so easily why another woman becomes depressed after giving birth to one. Often, too, the patient's despair is sharpened by the belief that the trouble is something beyond understanding or in the category of insanity—something which isolates him from the fellowship of other men. If you can dimly imagine what it is like to find your most valued relationships with other people collapsing, a gulf of hopeless misunderstanding widening between you and others, and even your esteem for yourself turning to abhorrence, you can begin to see why people may do appalling things in psychiatric crises and why it is difficult to persuade them that you mean to help them and that you have any ability to help.

Investigation and Treatment Measures

In the second stage of dealing with a psychiatric emergency, it has been recognized but not yet analyzed as to what it is about, what life-process it belongs to. The task in this stage is to combine psychiatric first aid with investigation which will enable the physician to give more specific help. When skillfully conducted, investigation and first aid assist one another rather than interfere. Having conveyed to the patient, and to whomever is involved with him in the emergency—perhaps it involves a couple, or a small group—that you are taking the situation seriously and that you aim to help, you then invite those concerned to turn from any rash action or extravagant emotion in which they are engaged, or to rouse from discouraged inaction, and to assist by describing, recounting, explaining, and considering the emergency and its origin. You invite them, in short, to join you in talking and thinking. If they do so, the emergency at least is over, for thoughtful discussion is diametrically opposed to psychiatric emergency. Of course, it is usually not so easy. Then, by remaining on the scene and showing interest, you maintain yourself as a new factor in whatever disturbance between people constituted the emergency. People tend to quiet down when they are around others who keep calm; if you can avoid being caught up in the excitement, you will tend to calm the others, who will thereby be better able to explain, listen, and think. Some people automatically become calmer—not tensely controlled, but relaxed—when others are excited; if you happen to be one of those, you should be a good man for emergencies. Administration of sedatives, including tranquilizers, may be helpful and is sometimes necessary; apart from their biochemical effect, they have an important placebo effect, especially in emergencies.

The prescribing of sedatives is a crutch for the physician, and each owes it to his professional self-esteem to discover how effectively as a sedative his personal influence can be. You may find that you have been giving some drug the credit which properly belongs to yourself. At any rate, you, as a new factor in the situation, will be tending to calm it down or to activate it, whichever it may seem to need, and to inquire about it. As you mold the situation toward being an inquiry, you will begin to gain information about what is and has been going on. You gain that partly from the mere words and sentences that could be printed, but mainly from all the nuances of speech, the gestures, facial expressions, changes of position, and the like.

As you begin to catch on to what has been happening, you may perceive that the crisis consists of an extraordinary emotional display—extraordinary in degree or in kind of expression but understandable as a reaction to the circumstances disclosed. Usually the mere joint acceptance of such a display as understandable reduces its violence; at any rate, once it is clear that certain given circumstances have to be dealt with, it is usually possible to imagine some other and more satisfactory methods. As you go on with your inquiry and discussion, such alternatives may occur to the people you are trying to help, or you may suggest them, by tactful hints if those are enough, or directly if need be. What I have said to this point spells out the *meaning* of the commonly used term "supportive treatment" as it applies to psychiatric emergencies. It amounts to doing for people most of what they are unable to do for themselves, along the lines of self-control, observation, thinking things out, and initiating helpful action. The physician should offer support in emergencies up to a point which gives relief but leaves the people concerned to do as much as they can for themselves. At that point, of course, the physician will still be hearing some complaints and requests rather than expressions of complete satisfaction but he will be able to stop there if he can remember that some residual dissatisfaction with the help obtained from others will in the long run stimulate the patient's own initiative, even though it makes a less glorious achievement for the physician at the moment.

If the emergency turns out not to be understandable as a reaction to the preceding social circumstances, if the patient does not begin to move toward accepting help and clarifying the needs and objections that led to the emergency, then the physician and such other responsible helpers as can be found must take control, safeguarding the patient with their best understanding and foresight against his expressed will, if necessary, as one would deal firmly and gently with a terrified child.

The physician's task is to minimize the harm that may occur; the patient should not be allowed to injure himself or others, to do major damage to property, or to assume tasks in which his whims or negligence might be dangerous or costly. Sometimes a person who is too disordered to discuss his condition intelligibly can still be persuaded in simple terms that he needs care and should be cooperative. If drugs are given or restraints used, it should be done without increasing the patient's fears, if possible; gentle restraint by the hands of a familiar relative or friend is much less frightening than being handcuffed or locked up. It is sometimes difficult to persuade relatives that a person is really mentally *ill* and should be taken to a psychiatrist or to a psychiatric hospital. Their refusal to understand is most irritating, because the physician himself is likely to be nervous in dealing with the psychiatric emergency. It is perfectly respectable to be nervous; if you can be a bit indulgent toward your own nervousness, and if you can remember that the patient's illness is usually also present in the relatives, only less spectacularly, you will find that you can tolerate and manage their impracticality much better.

If several psychiatrists practice in the community, they can naturally be considered as a resource to be called on when an emergency demands more psychiatric skill than the physician himself possesses. You may be shocked, and understandably resentful, if in some tight spot you find that the ones you call have no time to see your alarmingly upset patient that day or perhaps for several days. Why can they not make time for emergencies as other specialists do? In one type of psychiatric practice it is in fact difficult to find time, but there are other types of practice, and one can find out which of the available psychiatrists usually have time for emergencies—some because they prefer that sort of practice and some because their time is not yet taken up with psychotherapeutic patients. Many nonpsychiatric physicians are still more or less uneasy in psychiatric territory and tend to avoid psychiatric patients, psychiatric ideas, and psychiatrists. As a result, an inescapable psychiatric problem catches them unhappily ignorant of their own and the community's resources and, not uncommonly, they relieve their sore feelings by condemning everything psychiatric. Unfortunately, that sort of relief leaves them as ignorant as before, and they are pushovers for the next psychiatric problem that comes along. If anything keeps bothering you, it is much wiser to investigate it than to keep denying it; every surgeon knows that, and it is equally true in psychiatric matters.

SOME COMMON DENOMINATORS OF HUMAN EMERGENCIES

Charles E. Goshen

When the terms "psychiatry" and "psychiatric patient" are brought up, there is likely to be an assumption on the part of the general physician that only a special class of patients is meant which he is likely to come in contact with only on rare occasions. Such an assumption is made because, historically, the psychiatrist confined his interest to psychotic patients and was segregated from medical circles to such a degree that most physicians had only remote contact with him. During the past 20 years or so, however, psychiatry has moved out of the traditional confines of the mental hospital to tackle the problems of rather ordinary people in commonplace situations. Today human behavior in all its manifestations is as much a subject of psychiatric study as the bizarre and peculiar forms seen in state hospitals.

Similarly, the question of "psychiatric emergencies" can legitimately be considered as simply "human emergencies," some of which might be as complicated as a homosexual panic and others as commonplace as a child's nightmare. In spite of the fact that the various types might look strikingly different and some might seem frightfully difficult to comprehend, they all have much in common. The way in which they are more or less alike depends on the fact that the threats to human existence are rather limited in variety and tend to produce rather simple, elemental types of responses in all people. The way in which they tend to look much different from each other depends on the fact that people differ widely in the ways in which they interpret a given situation and the ways in which they express these individual interpretations.

Causes

First, the most obvious and important common denominator of human emergencies is the element of danger. The danger in question might have any one of the following qualities: (1) real danger; (2) danger which the patient is aware of or one that he is unaware of; (3) danger to him or danger to others; (4) danger to his biological existence or threat to his social existence.

Second, that which signals danger in humans is fear or alarm. Almost invariably the physician's attention is attracted to an emergency because someone has expressed alarm. This fear may not be expressed by the patient but by his family, friends, the police, nurses, or others. In order for this fear to be produced, there must first exist, in someone's mind, the idea that danger exists. It is elementary to note, but worth emphasizing, that fear will not be experienced by a human being until he has developed the idea that danger confronts him. The mere existence of danger is not enough to produce fear. The fact that it is the idea, and not the actual danger, which produces the fear explains many of the apparent mysteries of human behavior.

The types of danger possible can be conveniently divided into threats to one's biological existence, such as the discovery of cancer, or threats to one's social existence, such as impending divorce. Sometimes we make the mistake of minimizing the seriousness of the possible threats to social existence. In American society, however, the threat of social disgrace or loss of friends may have a more devastating effect on a person's morale than the threat of death itself.

There is another important emotion, other than fear, which can be, and often is, associated with human emergencies. This is the emotion of anger and is almost invariably involved with fear. Anger is the emotion experienced toward another person which results from the idea that the other person is endangering our existence. In other words, fear is a feeling about our own safety and anger is the feeling against the person who appears to be endangering our safety. Again, it is important to emphasize the fact that the idea of another person causing us danger must exist in the mind before anger is produced. As in the case of fear, the idea may be a correct one or an incorrect one. In other words, there can also be "imagined insult," as there can be "imagined danger." Because the unpleasantness of the emotion of fear demands some sort of action on the part of the person who experiences it, and because it is always based on the idea that danger exists, it is quite likely that a person might develop the idea that the danger is being produced by another person and become angry at him as a result. Therefore, it is not unusual to find fear and anger coexisting and, as a result, productive of some difficulty in sorting out which is which. The apparently complex problems in psychiatry, such as depressions and paranoia, appear complicated because of this mixture of fear and anger. To produce still further complications, anger itself can lead to fearful ideas of the consequences of one's anger, thus adding a new source of fear to the one which originally led to getting angry.

Management

Having looked into the cause and the manifestations of psychiatric emergencies, we might now examine the problem of management. Again, we will look at this problem from the point of view of the common denominators. We, as physicians who are presented with the problem of finding a solution to the emergency, are presented with certain allies and, on the other hand, certain obstacles.

Allies.—The allies are as follows: The resiliency of the human personality in coping with stress works to our advantage in the same way that the physician's greatest ally in treating organic illness is the natural healing capacity of the body. The presence of the patient's own resourcefulness, like the presence of the physiological healing process, is of sufficient importance that it behooves all of us to be humble about the influence we have on the course of the patient's problem. The interdependence of human beings is such that the mere presence and interest of other persons have a major role in one's overcoming emergency situations. Actually, most of these problems never reach the physician's office but are adequately alleviated by the simple proximity of other people. Time is such an important factor that it is almost always appropriate to recommend to the patient that, however serious the situation appears today, it probably will not seem so serious tomorrow. Time effects miracles, not through the process of forgetting but through the inevitable human proclivity to find other, new interests and activities to take the place of tragedy. There is always a good probability that the emergency problem will not turn out to be as catastrophic as it appears once more light is shed on the subject and the real truth discovered. People, in general, are likely to regard the physician as a wise person interested in helping. This becomes a tremendous asset in treating the patient.

Obstacles.—On the other hand, the physician is confronted with certain obstacles, some of which are as follows: The type of thinking and behavior which originally got the patient into his difficulties may be the kind which is likely to be repeated by the patient, thus perpetuating the trouble, or to bring about a recurrence. By the time a person seeks a physician's help, the difficulty has probably progressed to a more serious point than it would have been sometime earlier. The fear that colors most emergency situations tends to promote a paralysis which interferes with getting the patient to act. The person in serious trouble, whether real or imagined, is inclined to be suspicious of others, and it may be difficult, then, to obtain cooperation.

Principles of Management.—Taking into account our allies and our obstacles, we might define and list the principles of management which are appropriate to most, if not all, human emergencies.

Human Interest: Human interest, alone, is often sufficient to help a patient over the pain he experiences in the face of a real or imaginary emergency and to get him to rely on his own resources to solve the problem. The child with a nightmare, for example, needs nothing more than to be assured of the presence of interested adults in order to become oriented to the safety of reality in contrast to the dangers which had been apparent in phantasy.

Sympathy: Unfortunately, sympathy is something which is often abused but, nevertheless, something which can be helpful when appropriate. On the one hand, it would seem unprofessional for a physician to be unsympathetic but, since sympathy so often is construed to mean approval, we might find ourselves in a position of approving of something which is unreasonable. To avoid misunderstandings, it is important to make it clear to the patient that our sympathy is for the suffering he is going through and not for the factors which caused it.

Understanding: The patient and the uninformed are likely to regard understanding as meaning some sort of agreement. However, let us mean by "understanding" the collection of the true facts and the drawing of rational conclusions from them. Actually, real understanding might turn out to be an insult to the patient, for he may be trying to conceal the truth. However, once the problem is understood and is brought out into the open, it tends to put people in a position where they are forced to act more rationally than they would otherwise, even if such is not their wish.

Calmness: Without a doubt, the most reliable technique to a physician in the face of an emergency is calmness, meaning an unexcited, careful thoughtfulness. Calmness on the part of another person, especially when it is shown by a respected person, such as the physician, will nearly always quiet the excitement of others. True, the patient might put a physician through a test by behaving more excitedly, at first, but in the long run the calm approach will win out, simply because excitement fatigues itself and calmness does not.

Time: Either the patient or his family will generally demand some sort of immediate action in the face of an emergency, and the pressure thus brought to bear on the physician is probably responsible for more mistakes than any other single factor. It is necessary to realize, when a great deal is at stake, which is usually the situation in any emergency, that carefulness, not impulsiveness, is called for. In other words, in spite of the pressures exerted on us to act quickly, let us take our time to find out what the problem is all about and to carefully work out a way of solving it. Let us not rush to knock out the patient with sedatives or dump him in a hospital until we know enough about the problem to decide that such measures are necessary. Actually, they will seldom be found necessary when we take the time to uncover the truth.

PYELONEPHRITIS

IN DEFENSE OF THE URETHRAL CATHETER

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The urinary catheter must be respected. Its use is essential in many situations. In patients with debilitating general disease or obstructive urologic lesions it is not surprising when bacteriuria, pyelonephritis, or even bacteremia follow catheterization. The indwelling catheter must be expected to elicit a foreign-body reaction, and the cellular elements and bacteria sometimes persist in the urine as long as three months after removal of the catheter. Longer persistence should raise the question as to whether the urinary system is emptying efficiently. The hazards of using the catheter in a given case must be weighed against the probable consequences if it is not used. To be both safe and reliable, the technique of catheterization must be carried out aseptically. It demands adequate facilities, personnel, and preparation. It should be done with adequate exposure and good lighting, by two nurses or a physician and a nurse.

Pyelonephritis is the most common type of renal disease. In a chronic form it is a serious menace to life and health. Recently, some physicians have accused the catheter of being responsible for the occurrence of pyelonephritis and have inferred that the use of the catheter can have grave consequences. The urologist, whose professional life is intimately associated with the catheter and other instruments designed to explore and treat diseases of the urinary tract, probably has some opinions about these matters. The purpose of this paper is to comment on some aspects of the relationship of the catheter to pyelonephritis.

Urologists, whose experiences now cover a period of about 50 years as a specialty, have developed great respect for the possible dangers involved by, or consequences occurring after, the use of urethral instruments. Those who personally use urethral instruments rather constantly should be qualified to discuss the proper use of these instruments, provided their point of view is sufficiently broad to include the opinions of all who are studying the many aspects of urinary tract infection. The recent reports of Beeson,[1] Jawetz,[2] Kass,[3] and others on pyelonephritis are important, indeed, if properly evaluated and interpreted.

The catheter, in relation to its use in the urinary tract, may be in a similar position to the automobile in its relation to transportation of an individual person or his family. Each day people are killed by or in an automobile. These sad events are in the headlines. Caution and precaution are stressed to avoid the catastrophes associated with this vehicle. Yet many people find the daily necessities and conveniences of the automobile sufficient to warrant its continued use, on the basis that the benefits are greater than the dangers—in general.

In a discussion of the catheter and its possible affiliation with pyelonephritis, we have two main topics to expound—the disease and the instrument.

Review of Literature

An extensive bibliography exists on pyelonephritis. The pathogenesis, natural history, bacteriological considerations, symptoms, and treatment are fascinating aspects of this disease. We cannot add to the many fine treatises and résumés written by Beeson,[1] Bell,[4] Brewer,[5] Kass and Schneiderman,[6] Jackson and Grieble,[7] Jawetz,[2] Nesbit and Conger,[8] Weiss and Parker,[9] and others.

There are some published statements which seem to be pertinent to the discussion at hand. Because renal infection can develop via the ascending route (intraluminary or lymphatic) as well as via the hematogenous route, Beeson[1] has stressed bladder infection as a dangerous precursor of pyelonephritis, even though he has written that the risk of upper urinary tract infection after cystitis cannot be stated.

Bell[4] has said that the obstructive type of pyelonephritis is about 12 times as frequent as the nonobstructive type and that obstructive lesions in the urethra, prostate, and bladder promote infection of the kidneys about twice as often as obstructive lesions of the ureters above the bladder. He believes that, in the early stages of the disease, ascending and hematogenous pyelonephritis may be distinguished by examination of the kidneys but that this distinction can seldom be made in the advanced stages of the disease. He writes that the majority of patients with acute pyelonephritis recover, a few die, and a few develop chronic disease. Chronicity usually develops as the result of any anomaly which prevents drainage of the kidneys.

Birchall and Alexander[10] have said that pyelonephritis which terminates in renal insufficiency is rare compared with the general incidence of infection of the urinary tract.

Jackson and associates,[11] during a study of renal biopsies, demonstrated histological evidence of pyelonephritis in five of seven patients with symptoms of acute febrile urinary infection. Evidence of disease by biopsy was also present in 8 of 11 patients with a history of chronic urinary infection with intermittent acute flare-ups and in 12 of 18 patients with a history of chronic urinary infection who had no flare-up. The proportion of normal biopsies decreased in relation to the duration of symptoms. In four patients who had bacteriuria but who had no urinary or systemic symptoms results of renal biopsy were normal.

Weiss and Parker[9] found that it was often difficult to ascertain, either from the clinical or from the morphologic evidence, whether the inflammatory or the vascular lesions were primary in people dying of uremia or the complications of hypertension. They stated that the striking discrepancy between the large number of acute cases and the considerably smaller number of chronic cases of pyelonephritis indicated that acute pyelonephritis healed in the majority of instances. If the infection persists or recurs frequently, however, pyelonephritis becomes a disease of grave prognostic significance.

In an important autopsy study of the relationship between bacteriuria and pyelonephritis, MacDonald and associates[12] found that in 100 autopsies 53 showed no bacteria in the bladder urine, 7 showed only 10 to 100,000 bacteria per milliliter of urine, and 40 showed more than 100,000 bacteria per milliliter of urine. Of the 40 patients with gross bacteriuria, 17, or 42%, showed active renal infection. The authors state that definite conclusions concerning the manner in which bacteriuria is related to pyelonephritis cannot be drawn from their study and that a reliable clinical method for determining which of the patients with bacteriuria have renal involvement remains to be explored. It is also fair to say that they implicate the catheter as a possible or probable factor causing bacteriuria and pyelonephritis.

As early as 1915 Brewer[5] did experimental work in dogs by injecting bacteria intravenously and demonstrated that inflammatory lesions of the kidney followed only when there was a prior man-made injury to the kidney.

More recently, Beeson, Rocha, and Guze[13] again demonstrated that, in experimental animals, pyelonephritis does not develop after introduction of coliform bacilli into the urinary passages or into the blood stream unless the kidney has been previously obstructed or traumatized.

From the above opinions of outstanding authors on the subject of pyelonephritis, one might summarize as follows. Pyelonephritis occurs much more frequently in patients who have an anatomic variation in the lower urinary tract which causes obstruction than in patients who show no structural alteration in the urinary tract. Pyelonephritis is much more common in persons who have diabetes or other systemic disease. Acute pyelonephritis can arise from bacterial invasion of the kidney either via the blood stream or via ascending pathways from the bladder. Patients with acute pyelonephritis usually recover, but there are some who, because of recurrent infection, will develop chronic pyelonephritis and renal failure.

The physician has the following responsibilities in regard to any patient with urinary tract infection. He should avoid measures or procedures that might facilitate the development of pyelonephritis, such as instrumentation in the presence of acute infection. He should treat, by surgery if necessary, any anatomic variation which may contribute to recurrent infection. He should regulate systemic disease by the best methods available. He should treat the urinary infection medically in a thorough manner with frequent and sufficiently long follow-up observations to avoid chronic renal disease.

The Catheter and Its Relationship to Urinary Infection

The second section of this paper deals with the catheter in its relation to urinary infection and thus directly or indirectly to pyelonephritis.

In past years, the definition of urinary infection by bacteriological methods has not been as simple as one might suppose. For example, does a positive qualitative culture demonstrating organisms establish a diagnosis of urinary infection? Is it normal or abnormal to have a few bacteria in the urine? Does a positive culture represent a true urinary infection or does it represent contamination from the urethra or from the technique of the test?

At present, a quantitative report of urine cultures, rather than a qualitative report, is believed necessary to prove that there is significant urinary infection. Quantitative culture reports are standard laboratory procedure today in the study of urinary infection. Guze and Beeson[14] concluded that the use of a liquid culture medium does not yield information on the number of bacteria originally present in the urine and recommend the use of plates for quantitative reports.

Sanford and associates[15] have stated that a degree of bacteriuria of over 1,000 viable organisms per milliliter of urine is required for a valid diagnosis of infection. On the basis of 250 cultures, they found that approximately 5,000 to 10,000 viable organisms per milliliter had to be present before the bacteria could be seen on the stained smear of the centrifuged sediment. Jawetz[2] also agrees that numbers of bacteria in excess of 500 to 1,000 per milliliter of urine are necessary before the physician can state that there is urinary infection. MacDonald and associates[12] found more than 100,000 bacteria per milliliter of urine in patients with active pyelonephritis.

Quantitative cultures or microscopic demonstration of bacteria seem to be required to establish a diagnosis of active urinary tract infection. This standard or concept invalidates many of the older bacteriological studies about the incidence of urinary infection in various groups of persons (infants, pregnant women, and postoperative patients).

The next question is: How should the urine specimen be obtained? The clean voided specimen from male or female will be satisfactory if the first 20 to 30 ml. of urine are not used. By this method one hopes to avoid contaminating organisms which are normally present in the urethra.

In the female patient, a catheterized specimen of urine is and has been commonly used for culture studies. Here again it is important not to include the first 20 to 30 ml. of urine if one is to avoid urethral contamination. Guze and Beeson[14] cultured the tips of catheters after they had been inserted into the urethras of 13 female patients and obtained some bacterial growth in six cultures. In 12 patients undergoing laparotomy they compared cultures of bladder urine obtained from the bladder by needle aspiration to catheterized specimens after operation from the same patients; in 8 patients both samples showed no growth, and in 4 the aspirated specimen showed no growth while the catheterized specimen grew bacteria in fewer than 100 colonies per milliliter.

Monzon and associates[16] recently made a comparative study of urine specimens obtained by needle aspiration of the bladder, catheterization, and midstream voided methods in 34 patients. According to table 1 in their paper, of 27 patients with sterile cultures of aspirated specimens, in 7 the cultures from the catheterized specimens showed minimal growth (2 to 54 colonies per milliliter) and the midstream voided specimens showed somewhat larger counts (100 to 400 colonies per milliliter). Of 15 patients with negative cultures of the catheterized specimen, in 12 (80%) the cultures from the midstream voided specimens showed some growth. The authors believe that colony counts below 100,000 bacteria per milliliter of urine represent urethral contamination.

On the basis of a quantitative concept of cultures it would appear to us that either the catheterized or midstream voided urine specimen is reliable to demonstrate the presence or absence of real urinary infection. However, if one were to limit culture studies on the urine to qualitative methods, there could be an 80% error in using midstream voided samples instead of catheter specimens.

Jawetz[2] believes that, in female patients, urine specimens for satisfactory culture determination must usually be obtained by catheterization.

Is there danger of introducing infection to the bladder when catheterization is used to obtain the specimen? Jackson and Grieble[7] made a study of 58 ambulatory patients who were catheterized a total of 169 times at intervals of two to four weeks. By the criterion of quantitative bacteriuria, the maximum rate of infection induced by repeated intermittent catheterization in the outpatient clinic was 3%. From this study they concluded that intermittent catheterization in their outpatient department does not appear to be a significant factor in the pathogenesis of pyelonephritis.

At this point one might comment on how variable circumstances can influence the reliability as well as the dangers of catheterization. It is our impression that the incidence of cystitis after catheterization is even lower in office or clinic patients than in hospital patients confined to bed. The office patient rests on an examining table which insures a proper position for adequate exposure of the introitus. Perfect light is available. The procedure is carried out by two nurses, or a doctor and a nurse, one assisting the other, and it can be done easily and aseptically.

In contrast, a hospital patient is confined to bed. It may be 10 p. m. and the floor shorthanded. The patient in distress may be an obese woman who has not voided after surgery. The nurse comes to do her duty. She is unassisted. She gets the patient in position and places a lamp at the bedside. The heavy buttocks of the patient, showing the effects of rich American living, sink into the mattress and obscure the introitus. The nurse dons her sterile gloves and peers down at the limited and obscure operative field. Aroused by apprehension at all of this preparation, or because of discomfort, the patient moves one leg and knocks the lamp to one side. With her elbow, the nurse nudges the lamp back into fairly good position as best she can and continues her work in semidarkness. Unable to see the urethral meatus clearly, she makes several probing tries with the catheter, unavoidably contacting what now may be a contaminated area, before the urethra is found, urine flows, and both patient and nurse take a deep breath, signifying relief. In this situation, the specimen may not be reliable for culture and bacteria may have been introduced into the bladder. To be both safe and reliable, the technique of catheterization demands adequate facilities and personnel.

In 1955 Beeson[1] wrote that the risk of upper urinary tract infection after cystitis had not been determined. Three years later Beeson[17] reported that infection of the bladder not infrequently results from catheterization and that this can lead to pyelonephritis.

We believe that anyone who has used catheters during a lifetime of urologic practice knows the following statements to be true. Nontraumatic sterile catheterization, with use of a small catheter through a properly cleansed field, is rarely followed by urinary infection in the patient who is ambulatory and who empties the bladder efficiently. Catheterization of a bed patient in good condition and who is voiding well carries a minimal risk of infection. Repeated catheterization of the ambulatory or bed patient who is not emptying the bladder will probably be followed by at least lower urinary tract infection (cystitis), whether the inefficient voiding is caused by general disease and debility or by local anatomic disease of the urinary tract. Catheterization through an acutely infected urethra or through an obstructive urethral lesion may well produce a temporary bacteriemia with resultant acute pyelonephritis. Some of the general statements regarding the dangers of urinary infection after catheterization, as stated in the recent medical literature on pyelonephritis, are definitely misleading.

One should have respect for the catheter and use it judiciously, obtaining proper urine specimens without fear of complications in some circumstances, as just mentioned, while in other circumstances weighing its possible usefulness against the probable consequences if it is not used. Again comparing the use of the catheter to the use of the automobile, let us say that if the vehicle is operated properly amidst excellent traffic and weather conditions, travel will be completed without undue risk. If it is improperly operated or operated during hazardous traffic or weather conditions, a smashed fender or worse is likely to follow.

Catheter for Constant Drainage

The use of the catheter for constant drainage of the bladder has been said to contribute to development of urinary infection. Kass and Schneiderman[6] recently reported an interesting study on three semicomatose patients who required constant drainage. Several days after a strain of Serratia marcescens, a motile gram-negative bacillus nonpathogenic to man, was applied to the urethral mucosa near the external meatus, bacteria of the same type were recovered in the urine draining through the catheter. They suggested that entry of the organisms into the urinary bladder was effected via the urethral fluid, composed of urine and exudate which usually forms around the catheter.

No one can have any doubt that catheterization or other instrumentation of the infected urinary system is prone to produce an acute febrile response, probably caused by a bacteremia. However, clinical experience has indicated innumerable times that chronic pyelonephritis does not necessarily follow.

Related to the above remarks about the urethra as a place of septic absorption and traffic for bacteria, but in a way distinct from that concept, is the fact that most patients who require constant drainage with an urethral catheter for more than a few days show evidence of cystitis with bacteria in the urine from the bladder. In the past, it has been common urologic knowledge that, even with sulfonamides or antibiotic therapy given systemically and bladder irrigations done locally, the bacteriuria during a period of constant drainage could not be entirely eliminated. Because many patients who may require catheter drainage as part of a urologic operation enter the hospital free of urinary infection, some authors have stressed the nosocomial infections that begin during hospitalization, and they have therefore acquired a hostile attitude toward the catheter.

MacDonald and associates[12] concluded that the use of an inlying catheter is a ready means whereby bacteriuria may be induced, and we agree; but we doubt their statement that the catheter may play an important part in the development of pyelonephritis.

With acknowledgment that lower urinary tract infection during a prolonged period of catheter drainage is common, let us consider the explanation and significance of this situation. The catheter is a foreign body. A foreign-body reaction in the adjacent tissue is unavoidable. The mucosa of the urethra and bladder become congested and provide a fertile field for bacterial growth, and this may be destined to continue as long as the catheter is necessary. Furthermore, in patients who require surgery involving the prostate or bladder, traumatized tissue offers an additional excellent medium for bacterial growth.

Talbot and associates[18] recently completed a survey of 50 patients who had required catheter drainage from 1 to 14 years. Although all had bacteriuria, 72% showed no clinical evidence of renal disease as determined by laboratory tests and intravenous pyelography. They concluded that it is not so much the indwelling catheter as the development of an obstructive lesion in the upper urinary tract that leads to significant renal infection.

The significance of bacteriuria during constant drainage of the bladder by catheter is not as horrid as some writers infer. Although every possible effort should be made toward a bacteria-free urine while the catheter is in place, we believe the most important question is whether or not the urinary infection remains to plague the patient after the catheter has been removed. How long does it take for the urine to clear itself of cellular elements and bacteria after operations on the bladder and prostate in which the catheter has necessarily been used for constant drainage? A period of three months is not unusual. Thus, in patients who have had urologic surgery, one should not pass final judgment regarding induced catheter infection until 90 days after operation. In all patients who have had catheter drainage, the ultimate presence or absence of bacteriuria will depend in most instances on whether or not the urinary system empties efficiently.

Furthermore, the incidence of acute pyelonephritis as determined by clinical diagnosis is not high during the period of catheter drainage or during the immediate postcatheter period unless the patient is debilitated from systemic disease or has obstructive uropathy. The incidence of chronic pyelonephritis on the basis of catheter-induced infection must be minimal indeed.

Summary

In summary, one can say that pyelonephritis is most common in children or adults who are ill with systemic disease or in those persons who have obstructive lesions in the urinary tract, although it does occur in patients who are in good general condition and have no structural disease of the bladder, prostate, ureters, or kidneys. Chronic pyelonephritis does not commonly result from one attack of acute pyelonephritis.

The catheter, properly used, can be employed safely to obtain a specimen of urine without danger of introducing infection in patients who are voiding efficiently. Use of the catheter intermittently in the debilitated patient or in those who are not voiding effectively can lead to serious urinary tract infection.

Use of the catheter for constant drainage of the bladder is frequently accompanied by bacteriuria because of foreign-body reaction and the introduction of bacteria into the bladder. The indwelling urethral catheter can be used for a long time in a patient in good general condition and with a normal upper urinary tract without undue risk of pyelonephritis.

The final estimate as to the presence or absence of urinary infection must be made at a time when the tissues involved have had time to recover from foreign-body reaction or surgery.

We find no evidence to implicate the catheter as a significant factor in the cause of chronic pyelonephritis. No doubt the majority of patients who develop acute pyelonephritis have never been catheterized prior to the onset of the acute infection. It is not logical to blame the catheter as a major contributor to serious urinary tract infections (unless it has been used improperly) simply because the instrument has been used as a diagnostic or therapeutic agent in patients with urinary tract disease. The catheter, properly used, is one of man's best friends.

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INNOVATIONS IN HOSPITAL CARE OF NEWBORN INFANTS

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Experience with cross-infections in hospital nurseries, especially with infectious diarrhea, has led to the conviction that anything which enters the mouth or nose of a newborn infant must be sterile and that the chief source of a cross-infection is the contaminated hand. Thorough handwashing is an important factor in preventing the transmission of disease. The technique here recommended is effective, while avoiding the excessive irritation of the skin often caused by older methods. The imminent hazards of rows of contiguous bassinets in nurseries are avoided by rooming-in, the ultimate aim being to transfer the newborn infant to a cubicled bassinet adjacent to the mother's room as soon as feasible.

Through the years nurseries for newborn infants have been intermittently plagued with cross-infections from two sources—hand-borne and airborne. Customary precautionary measures have often failed to prevent the sporadic appearance and rapid spread of infection from a sick infant to adjacent well infants. Those who experienced these nursery endemics and knew what havoc they cause realized the importance of stringent aseptic precautions. Such nursery banes have harassed obstetricians, pediatricians, and public health officials alike.

Recently an increasing number of maternity hospitals in the United States have instituted several radical changes in their long-established routines for care of the newborn infant. The primary aim for the use of antiseptic skin detergents for handwashing and in the bathing of newborn infants, as well as for rooming-in (complete or modified), is to eliminate or at least decrease serious endemics such as hand-borne infectious diarrhea and airborne staphylococcic respiratory infections. During the 19th century Oliver Wendell Holmes, Ignaz Semmelweis, and Joseph Lister, each in his own way, brought increasingly convincing evidence that contaminated hands can spread serious infections to well persons.

Infectious Diarrhea of Newborn Infants

Endemic diarrhea of newborn infants is exceedingly communicable and in many instances rapidly fatal. Local health authorities must be notified promptly, as soon as the first case appears, so that the most stringent precautionary measures can be put into effect. Rooming-in of all the other newborn infants with their mothers then becomes obligatory.

At the Cradle, in Evanston, in spite of what for six years had been considered a superior nursery technique, infectious diarrhea broke out in 1927. Of 80 infants who contracted the disease, 27 died—a mortality of 33%! Dick and associates[1] conducted exhaustive bacteriological investigations. They isolated Proteus morgani from the minute ulcers in the lower part of the intestine, reproduced the disease in laboratory animals with pure cultures, and produced diarrhea by inoculation of the sterile

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culture filtrate. Soon thereafter, Dr. G. Dick[2] evolved an aseptic nursery and milk kitchen technique. Since 1927 there have been over 6,500 admissions. Except for minor modifications from time to time, the technique has been in use for over 30 years. Although two minor instances of hand-borne cross-infection occurred, no death was due to infectious diarrhea contracted after admission. This flawless technique is based on the following credo: Anything that enters the mouth or nose of a newborn infant must be sterile; the chief source of cross-infection is the contaminated hand.

Prevention of Hand-borne Cross-infections

Before a newborn infant is attended by nurse, physician, or other personnel, it is imperative that hands and forearms be adequately cleansed. This is well stressed in a booklet published by the American Academy of Pediatrics.[3] In recent years diverse hand-washing techniques have been evolved by various health organizations, maternity hospitals, and purveyors of antiseptic skin detergents. Although unanimity does not yet exist, many health authorities and hospitals are in accord with the technique described in the well-illustrated "Guide for the Prevention and Control of Infections in Hospitals,"[4] published by the New York State Department of Health and the American Public Health Association. The following excerpts outline basic principles for giving individual care to any patient:

> Thorough handwashing is undoubtedly one of the most important factors in preventing the transmission of disease.
>
> Sinks with foot or knee controls, preferably foot controls, and a constant supply of hot and cold water, mild soap or detergent, and absorbent paper towels are essential.
>
> Extensive studies on the efficacy of some of the newer detergents, particularly those containing hexachlorophene, in handwashing indicate that these substances are more efficient and more rapid in action than are the usual neutral soaps.
>
> The use of a brush* is not advised because it may irritate the skin when hands are washed as often as they should be in patient care.
>
> Procedure:
>
> Time required—approximately 90 seconds.
>
> 1. Standing well away from the sink, turn on water to temperature comfortable to hands.
> 2. Moisten hands and apply a heavy lather of soap, covering well beyond the area contaminated. Pay particular attention to the areas between and under the nails. (Toothpicks may be provided for cleaning under the nails.)
> 3. Use friction, one hand upon the other.
> 4. Rinse thoroughly under running water, allowing water to flow from above toward the finger tips.†
> 5. Repeat 2 through 4.
> 6. Dry hands thoroughly.
>
> *Some hospitals advise the use of the sterile brush, especially for the initial scrub, at least for the cleansing of the nails, and whenever hands are known to be contaminated or are visibly soiled.
>
> †Some authorities maintain that it is safer to allow excess water to drip off at elbows (with arms bent and hands raised) and to dry with sterile or clean paper towels starting at finger tips and ending at elbows.

The primary aim for an abridged hand-washing technique is to save time, but safety must not be sacrificed. There is very meager clinically controlled evidence to prove superiority of hexachlorophene (G-11) liquid detergents over ordinary neutral soap and tepid water. No endemic of infectious diarrhea has come to an abrupt end solely as the result of substituting an antiseptic skin detergent for a neutral soap in hand-washing. Purveyors maintain that repeated daily use leaves an antiseptic film on the skin's surface. However, a far greater number of instances of irritation of the skin have accumulated than from the use of plain soap and tepid water. When excessive irritation of forearms or hands persists, the detergent should be used more sparingly or temporarily omitted, or there should be less energetic friction and prolonged rinsing with cold water, and wiping dry should be gentle.

Respiratory Cross-infections

Respiratory cross-infections of newborn infants are usually seasonal and are contracted in the nursery by the aspiration of viral or bacterial pathogens disseminated into the air by an infected infant, attendant, or mother, or the respiratory pathogen is aspirated while the infant is transported through a drafty corridor during a to-and-fro trip from the general nursery to the mother or back to the nursery.

Rooming-in and Its Advantages

It has long been known that, despite hygienic measures, isolation techniques, and quarantine, newborn infants in general nurseries and foundling homes are more prone to serious infections than those in private homes. Rows of contiguous bassinets in nurseries for newborn infants connote ever-present imminent hazards. Rooming-in (complete, modified, or obligatory) is an attempt to decrease needless risks. The ultimate aim should be to transfer the newborn infant to a cubicled bassinet adjacent to the mother's room as soon as the well-being of the mother and infant warrants. This can usually be determined within 48 hours. The prematurely born infants and those requiring special care should go to allocated nurseries directly from the delivery room. Aseptic hand technique must be observed at all times by all who attend newborn infants. To decrease airborne infections, the door to the infant's cubicle should be kept closed and visitors should be excluded while the infant is in the mother's room.

Shortly before the newborn infant is transferred to the cubicled bassinet adjacent to the mother's bed, the nurse in charge should explain to her, in a rather casual way, that the primary aim is to prevent infection to her and to her infant and that rooming-in is an added safety measure against hand-borne and airborne cross-infections.

In the past much of the nurses' precious time was devoted to the menial chore of transporting the infant from nursery to mother and vice versa. (Because of the recent shortage of graduate nurses, some hospitals have delegated much of the care in nurseries for newborn infants to transient, semitrained personnel instructed only in the rudiments of aseptic precautions.) Rooming-in has, to a great measure, eliminated this procession with its hidden risks. The primipara now has an opportunity to acquire first-hand information from the skilled nurses who now have more time at their disposal. The mother can be told how to care for her newborn infant, can see at first hand how to do it, and, most important of all, have the privilege of doing it herself—under supervision.

The prematurely born infants and the infants who require special care cannot be transferred to their cubicles. Occasionally their mothers express concern to nurses and physicians, despite repeated assurances of the well-being of the child.

Occasionally a multipara, anticipating a few restful nights before returning home, becomes disturbed by the nocturnal cry of an adjacent infant—perhaps not her own. Sound-proofing of cubicle ceiling and walls should be the solution.

To return the well infant from the cubicle to the general nursery each night increases the infant's chances of contracting a cross-infection, adds menial work to that of skilled nurses, and requires time that could be spent to greater advantage to both mother and child.

Summary

Hand-washing should rid the exposed skin surface of pathogens so that the newborn infant cannot become infected by contact. Irritation to nurses' arms from antiseptic skin detergent should decrease with less energetic friction, more rinsing in cold water, and gentle drying. Rooming-in should decrease cross-infections in newborn infants and give more time for nurses to instruct mothers in infant care. Inconveniences to mothers created by rooming-in are minor compared to the added safety. Sound-proofing of cubicle ceilings and walls should decrease transmission of crying.

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PREMARITAL BLOOD TEST.—When, about 1935, the compulsory premarital blood test issue began to be pressed upon state legislatures and health departments, the cure of syphilis still involved upward of 18 months of injections, once a week, with arsenicals or other toxic drugs. These prolonged, expensive, and sometimes dangerous treatments were often strenuously resisted by syphilitic patients, who frequently regarded the treatment as worse than the disease itself. Today, a single injection of bicillin is effective. As a result, cooperation with medical and health authorities has improved tremendously. Moreover, it seems probable that some syphilis is cured accidentally through penicillin treatment of many nonvenereal infections....

The percentage decline has occurred equally in states without a compulsory premarital blood test law and in states with such a law. During the last decade, the infant death rate from syphilis declined by slightly more than 97 per cent in both compulsory and noncompulsory areas. Similarly, the reported morbidity rates in the primary and secondary stages of syphilis dropped in the compulsory areas by 93.5 per cent and in the noncompulsory by 93.3 per cent, from 1945 to 1956. These findings suggested that the compulsory premarital blood test laws exert very little influence on syphilis mortality and morbidity. Other factors such as prenatal blood testing, improved case finding, and particularly penicillin treatment have more likely been responsible for the rapid decline in syphilis.

Furthermore, premarital blood testing reveals so few infectious cases of syphilis as to make it an unproductive method of case findings as well as an enormously expensive one. Added to these deficiencies, is the increasing problem of false-positive reactions in blood tests, a problem which will become even more serious as syphilis declines further.—A. W. Hedrich, Sc.D., and Charlotte Silverman, M.D., Should the Premarital Blood Test Be Compulsory? *Journal of Public Health,* February, 1958.

CEREBRAL MANIFESTATIONS OF VITAMIN B_{12} DEFICIENCY

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Pernicious anemia is associated with a subacute degeneration of the brain that is essentially the same as the more familiar subacute degeneration of the spinal cord. The pathological process is unique and easily distinguished from pellagra and other diseases involving the cerebral white matter, but there is nothing consistently characteristic about the resultant mental symptoms, and they may appear years before the anemia. These facts are illustrated in the case history of a 44-year-old housewife who suffered a severe mental disturbance with paranoid symptoms so severe as to necessitate institutional treatment. Ultimately all symptomatic therapy was discontinued, and intramuscular injections of vitamin B_{12} sufficed to bring about a complete mental restoration. Since none of the mental symptoms is distinctive and the blood changes may appear late, the early diagnosis depends on the physician's alertness to this possibility. Early treatment is necessary because the degenerative changes can be completely reversed only if they are recognized in time.

Mental changes resulting from vitamin B_{12} deficiency are among the least publicized aspects of this condition. The cerebral manifestations of this disorder have received little consideration in standard textbooks on the subject, although Preobrajensky[1] described brain lesions which he believed to be due to pernicious anemia as early as 1902. From the clinical description, however, one cannot be certain that his case was indeed one of pernicious anemia. Pfeiffer[2] in 1915 reported the first unquestionable case of pernicious anemia in which mental symptoms were prominent. Clinically the patient was confused, inattentive, and drowsy. On postmortem examination Pfeiffer found degeneration of the medullated nerve fibers in the white matter of the frontal lobes and slight alteration of cortical nerve cells. A more detailed clinical description of the cerebral manifestations of pernicious anemia was made in 1927 by McAlpine,[3] who reported that "Mental changes occur not uncommonly in pernicious anemia. They range from states of depression accompanied by loss of mental energy to definite psychosis. They, like the nervous symptoms, may precede the characteristic changes in the blood by many months."

Since it has recently been pointed out that the reversibility of the mental aberrations attendant to vitamin B_{12} deficiency is dependent on the duration of the illness before the institution of effective therapy, the importance of early diagnosis becomes apparent. Holmes[4] reported a series of 14 cases of vitamin B_{12} deficiency in which the patients had well-marked cerebral symptoms. In all but two of these cases the mental symptoms disappeared or were greatly improved after intensive treatment. The two patients who did not respond had been psychotic inmates of a mental hospital for several months before treatment was initiated, and their psychoses had developed gradually and progressively over a period of seven to eight years. Early diagnosis, though of utmost importance, is at times difficult because the cerebral manifestations may occur in the presence of a completely normal blood picture and bone marrow. Even when anemia is present there may be no correlation between the degree of anemia and the severity of the cerebral manifestations. Irreversibility may result if one awaits the development of overt hematological signs before the institution of therapy.

Neuropathology

Pathological studies by Adams and Kubic[5] revealed that the important pathological changes consisted of a more or less diffuse, though uneven, degeneration of the white matter with relatively little or no proliferation of fibrous glia. Microscopic changes were found in the central and convolutional white matter of the cerebral hemispheres, in the cerebellar peduncles, and in the optic tracts near the chiasm. The microscopic changes consisted of degeneration of the white matter more pronounced perivascularly, with foci of degeneration ranging from 50 to 150μ in size. Involvement of axis cylinders as well as myelin sheaths was found. In the more involved areas there were numerous macrophages filled with fat. These authors also noted an increase in the number of astrocytes and oligodendrocytes throughout the white matter. This change was most marked just beneath the cortical gray matter. In contrast the nerve cells appeared essentially normal. The changes described were essentially the same as those found in subacute de-

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generation of the spinal cord. To date there have been no authentic reports of cases of subacute degeneration of the brain which have not been associated with spinal cord lesions. This pathological process is unique and easily distinguished from pellagra and other diseases involving the cerebral white matter. In subacute degeneration there is uneven degeneration of the fascicular gracilis, while in pellagra there is degeneration throughout. The degeneration of the cerebral white matter is prominent in subacute degeneration, while there is none in pellagra. A third striking difference is the lack of nerve cell involvement in subacute degeneration, as opposed to pellagra where the anterior horn cells and larger pyramidal cells are moderately involved. The order of involvement appears to be the posterior columns, followed by degeneration of the lateral and anterior columns, with involvement of the cerebral white matter being the final step.

Pathogenesis

The pathological degenerative process appears to be related to a decrease in cerebral metabolism as a result of the deficiency state, rather than as a result of the anemia per se. Scheinberg[6] (1951) estimated the oxygen consumption of the brain by the nitrous oxide method in 16 patients with pernicious anemia. He divided the patients into two groups, those with a hemoglobin level above 7 and those with a hemaglobin level below 7 Gm. per 100 cc. He found consistently low values of cerebral oxygen consumption in patients with cerebral manifestations of pernicious anemia as compared to normal controls and those with secondary anemia (blood loss). There was no correlation between the degree of anemia and the reduction in cerebral metabolism in patients with a hemoglobin level greater than 7 Gm. per 100 cc. There was, however, a good correlation between the degree of mental status aberrations and the degree of reduction of cerebral metabolism. Earl and associates[7] in 1953 estimated the blood pyruvate levels in patients with subacute combined degeneration in the fasting state and 60 and 90 minutes after the ingestion of a loading dose of glucose (100 Gm.). After 90 minutes he found that in untreated cases of pernicious anemia with no neurological signs the blood pyruvate level was normal; while those patients with neurological signs had pyruvate levels greater than normal. When the determinations were repeated after two weeks of intensive treatment with vitamin B_{12}, normal values were also obtained in those patients with neurological signs.

Clinical Manifestations

None of the mental symptoms seen in this condition are consistently characteristic; the symptoms are extremely variable and range from a mild mood disorder to overt psychotic behavior. The milder symptoms may be a slight mood disturbance or mental slowness with difficulty in concentrating and remembering. The symptoms may be much more severe, however, with violent maniacal behavior, severe agitation, stuporous depression, paranoid behavior, or the presence of overt visual and auditory hallucinations. On mental status examination, in those severely disturbed, one may find disturbances in affect, insight, associations, and thought processes, feeling abnormalities and depersonalization. When present these mental status findings make it difficult to distinguish this condition from schizophrenia.

Diagnosis and Treatment

When mental symptoms occur in combination with the classic symptoms of pernicious anemia—weakness, sore tongue, macrocytic anemia, and achlorhydria—the diagnosis is relatively easy. When a patient presents with mental symptoms and is found to have moderate anemia, achlorhydria, slight macrocytosis, and bilirubinemia and complains of various neurological symptoms, the diagnosis of pernicious anemia is exceedingly likely. The common neurological symptoms encountered are pins-and-needles sensations and paresthesias. The paresthesias are usually localized to the distal portions of the extremities and are symmetrical in distribution. A large variety of other peculiar sensations such as numbness, stiffness, feelings of heat and cold, formication, deadness, tightness, and shooting pains may be present. Loss of vibratory sense is the most consistent neurological sign. When the mental symptoms are prominent while the usual diagnostic criteria are absent or minimal, the diagnosis may not even be suspected. In such instances reliance must be placed on special tests. The estimation of the vitamin B_{12} level in the serum with the alga Euglena gracilis as the test organism has proved to be helpful. With use of this method, the normal B_{12} range is 150-1,000 mcg. per 100 cc., while in proved cases of pernicious anemia the range is 0-85 mcg. The Schilling test has also proved a valuable adjunct to diagnosis. This consists of administering an oral dose of radioactive vitamin B_{12} and measuring the amount excreted in the urine. When given orally, 0-3% is excreted in the urine by patients with pernicious anemia, while the normal excretion rates are 10-25%. Thus the ability to estimate the vitamin B_{12} level in the serum and the determination of the excretion rates of radioactive vitamin B_{12} in the urine afford a reliable diagnostic method. In those instances in which facilities are not available to perform the diagnostic procedures described above, a therapeutic test with vitamin B_{12} may prove helpful. When the therapeutic test is employed, it is important that the test be made with B_{12} alone and that the reticulocyte response be observed daily for 7 to 10 days until a positive or negative result has been obtained.

The most important factor influencing the response to treatment is the duration of the disease prior to the institution of therapy. Factors of little importance are the degree of anemia or the severity of cerebral manifestations. Much larger doses of vitamin B_{12} are needed for the treatment of the neurological and psychiatric manifestations of the deficiency than for maintenance of a normal blood cell count. Treatment consists of the intramuscular injection of 1,000 mcg. of vitamin B_{12}, followed by 500 mcg. twice weekly for one month. Subsequent therapy consists of the administration of 100 mcg. of vitamin B_{12} intramuscularly once a week for the next six months. Most improvement occurs during the first three to six months of therapy. Relapses during therapy are usually associated with infections and can be corrected by increasing the maintenance dose of vitamin B_{12}.

Report of a Case

A 44-year-old housewife was admitted to the Pratt Diagnostic Clinic–New England Center Hospital on Jan. 9, 1958, with a chief complaint of severe depression, marked psychomotor retardation, and paranoid ideas. The gradual onset of depression became apparent a year before admission, and there was a marked exacerbation of all symptoms two weeks prior to admission. Because of the severity of the depression the patient was given three electric shock treatments at another hospital without improvement before being admitted to the psychiatric service of the Pratt Diagnostic Clinic–New England Center Hospital for evaluation and therapy.

The history of the present illness obtained from the patient and her husband revealed that in the past year she had become self-conscious and despondent over the fact that she was losing her hair and felt she was an object of ridicule. She expressed the notion that when she was in social gatherings "especially bright lights were lit" or that "they always sat me near the lights." Finally she became quite withdrawn and ceased her participation in all activities. She was depressed and irritable, cried frequently, and was constantly fatigued.

While she was undergoing diagnostic studies in the outpatient department of another hospital in December, 1957, a marked change in her behavior was noted. She expressed the idea that "The doctor hypnotized me, I felt I was in a trance. My head was straight. I could not turn it. He made me say that I did not trust my husband." She was seen by another physician whom she thought put dope in her rectum and caused her to lose control of herself. While there she believed that her behavior was being controlled by some external force. At home she was confined to bed, where she continued to express ideas of influence and control. In this connection she stated that "I had to stare at the ceiling . . . I had to stare at the sun . . . I could only eat bread and tea . . . I could not sleep." At home she remained confined to bed, markedly limited her food intake, and did not sleep for the week preceding admission to the hospital.

Mental Status Examination.—On admission she was markedly retarded and resistive. She appeared tense and apprehensive; there was a rhythmical movement of her legs, and she would not look directly at the examiner. She spoke only in response to direct questions; many of her answers were only partial. She overtly expressed paranoid ideas. She stated she was pale because her "blood is being drained," and that she was weak because "you are sprinkling things on me." She was oriented as to time and place. Her attention span, however, was poor and she could not retell a short story. Her mood was depressed. Her affect paralleled her thought content.

Physical Examination.—The most prominent physical findings were a waxy, pallid skin, pale conjunctivas, smooth tongue, thinning of her hair, and bruises over her entire body. Vibratory sense was absent in the toes bilaterally. The deep tendon reflexes were hyperactive, otherwise no significant physical or neurological abnormalities were found.

Laboratory Findings.—Study of a peripheral blood smear showed some macrocytosis. The hemoglobin level was 11.8 Gm.; white blood cell count was 10,500 per cubic millimeter. On examination of the bone marrow the over-all picture was one of normoblastic hyperplasia with a few megaloblastic forms (these results reflected the patient's use of hematinics —containing liver, vitamin B_{12}, and iron). Gastric analysis after histamine injection revealed no free acid. The reticulocyte count was 4.7%. The prothrombin time was 17 seconds, 29%. Total bilirubin was 0.3%, bleeding time 2 minutes 50 seconds, 2 minutes 10 seconds. The serum B_{12} level was 28 mcg. (Normal range is 150-1,000 mcg. per 100 cc.) Schilling test results were as follows: 20-hour urinary excretion of vitamin B_{12} (radioactive cobalt), 0.5%. (Normal range is 10-25%.)

Hospital Course.—After admission the patient was given fluids intravenously because of the marked dehydration present. While she was undergoing diagnostic studies, to allay her apprehension, anxiety, and depression, symptomatic measures were employed. On this regimen some symptomatic improvement was noted. The patient became somewhat more alert and a little more cooperative. When the diagnosis became established on the seventh day, all symptomatic therapy was discontinued and intramuscular injections of vitamin B_{12} were begun. By the 11th hospital day the patient was alert, no longer appeared frightened or anxious, and showed little evidence of depression. Her appetite had markedly improved, her sleep was much less disturbed, and she no longer complained of fatigue. She showed concern about her personal appearance, applying rouge and lipstick for the first time. She also showed renewed interest in newspapers, radio, and television. She still expressed some paranoid ideas—stating that "my husband brought a television set to make my nerves worse." She expressed concern regarding "everyone giving me compliments." At the time of her discharge on the 16th day she was cheerful and optimistic about the future and eagerly anticipated returning home. After her discharge she received intramuscularly 100 mcg. of vitamin B_{12} weekly.

Follow-up Visits.—When seen in follow-up on Feb. 15, 1958, her only complaints were facile fatigability and coolness of her toes. She had been sleeping well, her appetite had been good, and she had begun to participate in social activities. On examination, though somewhat slow in her responses, she expressed no paranoid ideas. Her associations and thought content were normal. On neurological examination the deep tendon reflexes remained hyperactive and there was diminution in perception of vibrations (128 cps) only in the toes of the left foot.

When seen again on March 29, 1958, the patient stated that she was able to do all her housework without fatigue and she had enjoyed social activities. Her husband had noted no abnormal behavior. On examination she expressed no paranoid ideas; her thought content and associations were intact. She stated that she was happy about her improvement and her affect was appropriate. In short, she showed no abnormal mental status findings. On neurological examination the deep tendon reflexes were still hyperactive, but there was no longer evidence of diminution in vibratory perception.

Summary

It is extremely important to make an early diagnosis of mental disease due to vitamin B_{12} deficiency, since the reversibility of the mental aberra-

tions depends mainly on the duration of the illness before the institution of effective therapy. Much larger doses are needed for the treatment of the neurological and psychiatric manifestations of the deficiency than for maintenance of a normal blood cell count. Cerebral symptoms may precede the appearance of anemia by years, and many occur in the presence of a completely normal blood picture and bone marrow. The essential cerebral pathology consists of a more or less diffuse degeneration of the cerebral white matter with little or no proliferation of fibrous glia. The mental aberrations are related to the decrease in cerebral metabolism resulting from the deficiency state. Since none of the mental symptoms is consistently characteristic, the diagnosis depends first on the physician's awareness of the existence of the disorder and second, in the absence of anemia, on the determination of the vitamin B_{12} level in the serum and the use of the Schilling test. A representative case showed that the prompt institution of effective therapy resulted in the complete reversal of the mental aberration.

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MULTIPLE ECZEMATOUS SENSITIVITIES

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There are three distinct varieties of multiple eczematous sensitivities. In multiple nonspecific sensitivity there is heightened susceptibility to the primary irritant effect of many chemically and immunologically unrelated substances. In multiple primary specific allergic sensitivity there is a greater than average susceptibility to the development of allergic eczematous sensitizations. The third variety, multiple secondary specific allergic sensitivity, is based on an immunochemical relationship between the primary allergen and the secondary allergens, which must be so closely related that the sensitized cells react to them as if they were identical. The pattern of the body's response to multiple secondary eczematous sensitizations is relatively unpredictable for a given person; the variations are numerous and striking, and the more intense the degree of primary sensitivity the greater is the likelihood that multiple secondary sensitizations will occur.

A review of the past 20 years' literature reveals a dearth of detailed discussion on the general subject of multiple eczematous sensitivities. Apart from a few papers which touch on certain phases of this subject, such as those of Rostenberg and Sulzberger[1] and Sulzberger,[2] only one form of multiple eczematous sensitivity—cross-sensitization—has attracted much attention. This lack of detailed discussion is more surprising since multiple eczematous sensitivities are regularly encountered and, therefore, are of the greatest practical importance and theoretical interest.

Even though one must be mindful of the inadequacies of all schematic arrangements and should beware of all oversimplification, it appears useful to differentiate between three categories of multiple eczematous sensitivities, namely, multiple nonspecific sensitivities, multiple primary allergic sensitivities, and multiple secondary allergic sensitivities (cross-sensitizations). The principal character-

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istics of the three distinct varieties of multiple eczematous sensitivities are summarized in the table.

In discussions of multiple sensitivities the words "polyvalent" and "multivalent" have often been used. These words are derived from the chemical concept of valence, that is, the quality which determines the number of atoms or radicals with which any single atom or radical will unite chemically. This concept has been applied in immunology where one speaks of the valence of antibodies, but it is questionable whether it is wise to apply it in nonallergic sensitivities or in allergic sensitivities where antibodies cannot always be conclusively demonstrated.

Multiple Nonspecific Eczematous Sensitivity

In multiple nonspecific sensitivities there is heightened susceptibility to the primary irritant effect of many chemically and immunologically unrelated substances. This occurs in certain persons whose skin threshold for irritation is so low that normally nonirritant concentrations of some substances exert a primary irritant action. It is well to realize that knowledge regarding susceptibility to primary irritants is rudimentary. Recent publications once more confirm the findings of Rostenberg and Sulzberger [1] that reactivity to primary irritants varies greatly in different persons even under normal conditions. Gahlen,[3] for example, showed the wide variations of the threshold values at which mercuric chloride has a primary irritant effect in different persons. Even the 1:1,000 solution of mercuric chloride, which is commonly used for patch testing for allergic eczematous hypersensitivity, acts as a primary irritant in a small percentage of those tested. Wilson [4] observed positive reactions in 68% of normal subjects in tests with 10 standard substances. Many of these reactions were simple erythemas without vesiculations, but they are, nevertheless, an indication of an unusually great susceptibility to primary irritation in these persons. Similar results were obtained in studies of Gahlen [3] with 14 standard materials.

Characteristics of Multiple Eczematous Sensitivities

	Multiple *Nonspecific*	Multiple *Primary* Specific	Multiple *Secondary* Specific
Mechanism	Low threshold for effects of primary irritants; not an immunological phenomenon	Abnormal capacity to undergo primary allergic sensitizations	Capacity to develop allergic secondary or cross-sensitizations or primary sensitization to allergen which obligatorily produces cross-sensitizations
Role of nonspecific factors	Usually highly important	Sometimes contributory	Usually not contributory
Immunochemical relationship of materials producing multiple sensitivities	Usually none	Usually none	Always present
Duration of multiple sensitivities	Evanescent—weeks to months	Relatively persistent	Relatively persistent

Whether there is an over-all irritability to many different substances in such persons or whether such normal skins are more susceptible to primary irritation from some substances than from others is one of many important questions which at present cannot be definitely answered. Obviously, when the borderline of what is and what is not a primary irritant is not clearly defined, it may be difficult also to differentiate between primary irritant effects and reactions on the one hand and allergic effects and reactions on the other. The experienced dermatologist, of course, develops the ability to some extent to differentiate between these reactions on the basis of their morphologic features.

Apart from variations for which there is no explanation in nonspecific irritability among normal skins, certain known factors may contribute a suitable terrain for the development of multiple nonspecific sensitivities. Allergic or nonallergic irritation superimposed on eczematous eruptions is one of the most important. The persistent use of irritating therapeutic agents causes spread of the previously localized eczematous eruption. The spreading may at first be slight, but it gradually increases until eventually the eczematous eruption may become generalized. This is especially liable to happen when the physician fails to recognize that it is the topical treatment which he himself has prescribed that is causing his patient's eruption to become progressively worse.

In such cases if one carries out patch tests during the acute phase of the eruption one may elicit nonspecific positive reactions with normally nonirritating concentrations of many diverse materials. These reactions will often be clinically indistinguishable from allergic eczematous patch test reactions, since they do not ordinarily resemble the primary irritant reactions which are seen, for example, in patch tests with undiluted soap.

A case in point is that of a patient who had a psoriasiform eruption with a superimposed allergic contact dermatitis due to topical medicaments. When he was first seen, his eruption had already become widely disseminated and he required hospitalization. The possibility was under consideration that allergic hypersensitivity to clothing materials might have contributed to the generalization of his eruption. Therefore, patch tests were carried out with samples from his suits, socks, shoes, and other garments. A number of more or less strong reactions were elicited with these materials. However, after he was discharged from the hospital in a much improved condition he found that he could wear with impunity the very suits and socks which previously had produced positive reactions. About a year later patch tests with some of the identical materials were repeated. This time no positive reactions were elicited, whereas, previously, a brown suit had given a 2+ to 3+ reaction, a gray suit 3+ to 4+, and a blue suit 3+ to 4+.

Wilson[4] concluded from his results that increased irritability, as evidenced by false-positive reactions, may persist for three months after the subsidence of the rash in patients with eczematous reactions. Moreover, it appears possible that there are some persons who have a more or less permanently increased susceptibility to primary irritation.

Impaired alkali neutralization and alkali resistance, which have been elucidated in the excellent studies of Burckhardt,[5] are among the other factors which may contribute to the development of multiple nonspecific sensitizations. In recent years it has been demonstrated in persons who have eczematous eruptions that the pH of the skin tends to shift to the alkaline side in the affected sites as well as in unaffected areas.[6] This shift in skin pH is associated with an accelerated neutralization of acids at the skin surface. While this shift in pH may be a consequence rather than a cause of the eczematous eruption in these patients, it is, nevertheless, perhaps a factor favoring multiple nonspecific sensitizations. Disturbances in sweating, such as dyshydrosis, bacterial, viral, and mycotic infections, a seborrheic and psoriatic tendency, and photosensitization are among the other factors which must be considered potential contributors to multiple nonspecific sensitizations.

Another factor which may be highly important from the practical viewpoint is the acanthogenic effect of certain agents. ("Acanthosis" denotes a hyperplasia of the prickle cell layer of the epidermis; "acanthotic" describes a prickle cell layer which has become hyperplastic; and "acanthogenic" denotes the capacity to engender a hyperplasia of the prickle cell layer.) The substances which engender acanthosis increase skin irritability to primary irritants and to allergenic agents. Baer and associates[7] showed that guinea pigs' skin, when deliberately made acanthotic, responds histologically with eczema-like and blister-like changes to irritants and allergens which cannot be produced in nonacanthotic skin of the same guinea pigs. At the time these findings were reported, the authors speculated that perhaps the acanthogenic effect of these substances plays a role also in the genesis or persistence of eczematous eruptions in man. Recently, Skog[8] has shown that, indeed, this effect does occur in human skin. The reason why these observations may well be of prime importance is that some of the detergents used for laundry and household purposes have a pronounced acanthogenic action.

Multiple Allergic Eczematous Sensitivities—Primary

Multiple eczematous sensitizations which are based on a specific allergic mechanism, rather than on nonspecific irritability of the skin, fall into two distinct categories: multiple primary sensitizations and multiple secondary sensitizations. The terms primary and secondary sensitization have been coined[9] to describe the event when a substance produces allergic sensitization not only to itself (primary allergen and primary sensitization) but also to one or more immunochemically related agents (secondary allergens and secondary sensitizations).

Multiple primary allergic sensitizations to immunochemically unrelated allergens are usually seen in human beings who have a greater than average susceptibility to the development of allergic eczematous contact sensitizations. Those who have had much clinical experience with the allergic, eczematous, contact type of dermatitis have long recognized that patients who have or have had this type of eruption tend more to develop additional specific allergic eczematous sensitizations than do other patients with urticaria, psoriasis, atopic dermatitis, or other dermatoses. This clinical impression was substantiated many years ago by the investigations of Bloch,[10] Jaeger,[11] Sulzberger and Rostenberg,[12] and others. Rostenberg and Sulzberger, for example, showed that patients with allergic eczematous dermatitis were at least twice as sensitizable to dinitrochlorobenzene or paranitrosodimethylaniline than subjects with other allergic or nonallergic cutaneous eruptions.

In a more recent study, Gahlen[3] observed the incidence of positive patch test reactions elicited with 14 standard test materials of known eczematogenic potential, including paraphenylenediamine, nickel, chrome, formaldehyde, and turpentine in three groups of patients: subjects free from eczema, subjects with nonallergic eczema, and subjects with allergic eczema. His results clearly demonstrate a greater tendency to multiple eczematous sensitivities in subjects with allergic eczemas than in subjects with nonallergic eczemas or without eczematous eruptions.

Wilson[4] also elicited many more positive reactions in patch tests in patients with contact eczema than in patients with discoid (nummular) eczema and atopic dermatitis, while the smallest number were elicited in persons with normal skin. The relatively large number of positive reactions elicited in Wilson's subjects with atopic dermatitis is explained by the fact that he included follicular pustular noneczematous patch test responses as positive. Actually, of course, the susceptibility to true eczematous sensitization in patients with atopic dermatitis is no greater than in normal control subjects.

What produces increased susceptibility to multiple specific primary allergic sensitizations? Here we are almost as much in the dark as were Bloch and Jaeger when they first described the existence of these multiple sensitizations many years ago. It is likely that some of the contributory factors previously mentioned in connection with multiple nonspecific sensitization are operative also in creating the terrain for multiple allergic primary sensitization, especially alkali damage[5] and acanthogenic agents.[7] Although the hypothesis of genetically determined susceptibility to eczematous sensitization is surely the most probable, in man there is, as yet, no conclusive evidence that genetic factors are involved in susceptibility to this form of sensitization. Thus, subjects with a susceptibility to multiple eczematous primary sensitization cannot be compared with atopic persons who on a genetic basis tend toward the development of multiple allergic urticarial sensitizations and the production of thermolabile antibodies of the Prausnitz-Küstner variety.

Multiple Allergic Eczematous Sensitivities—Secondary

In the third category of multiple eczematous sensitizations are the multiple secondary allergic sensitizations. These are usually referred to as cross-sensitizations, and they are of great practical importance since they account for a large number of multiple sensitizations. They are based on an immunochemical relationship between the primary allergen and the secondary allergens.[13]

First, the primary allergen and the secondary allergens are so closely related immunochemically (i. e., they contain identical allergenic groups) that the sensitized cells (the presumptive antibodies in or on these cells) do not differentiate between them and thus react as if they were identical. Examples of these are multiple sensitizations to the various Rhus allergens, which are catechols with a 15-carbon triply unsaturated side chain.

Second, the primary allergen is converted (reduced, oxidized, or in other ways transformed) in the body into compounds which are identical with the secondary allergens or are so closely related to them that the sensitized cells do not differentiate between them and thus react as if they were identical, or the secondary allergen is converted in the body into a compound which is identical with the primary allergen or is so closely related to the primary allergen that the sensitized cells do not differentiate between them and thus react as if they were identical. For example, in primary sensitization to picric acid (trinitrophenol) the paranitro radical apparently is converted in the skin into a para-amino radical, thus giving rise to secondary sensitization to other compounds containing the para-aminophenyl radical, such as certain local anesthetics and dyes.

Third, both the primary and secondary allergens are converted in the body into compounds which are identical or are so closely related that the sensitized cells do not differentiate between them. As shown by Leifer and Steiner[14] in some cases of cross-sensitization, among halogenated hydroxyquinolines it appears that iodochlorhydroxyquin (Vioform), diiodohydroxyquin (Diodoquin), and chlorquinaldol (Sterosan) all are broken down to carboxylated pyridines (picolinic acid and quinolinic acid) and that these pyridines are the allergenic complex producing the multiple secondary sensitizations.

These examples are just a few among what might be an infinite number, for it is obvious that the potential for cross-sensitization exists in every single case of allergic contact dermatitis. This holds true not only for contacted allergenic materials but also for ingested and inhaled allergens. In support of this, Baer and Leider[15] have shown experimental evidence suggesting that the ingestion of azodyes in foods can bring on flare-ups of the eruption and of itching in patients with allergic hypersensitivity to paraphenylenediamine in hair- and fur dyes. Another example is the cross-sensitization between streptomycin and neomycin based on allergenically identical groupings recently described by Sidi and co-workers.[16] Their work would indicate that a patient who has developed an eczematous contact sensitization to neomycin is very likely to have an allergic reaction when he is exposed to streptomycin not only by contact but also by injection.

One of the most interesting features of multiple secondary eczematous sensitizations is that their pattern is relatively unpredictable for any particular person. The reasons for the striking differences in the patterns of multiple secondary sensitizations are unknown. The great variety of these cross-sensitization patterns resembles the well-known variety in human fingerprint patterns.

It has been shown that the more intense the degree of primary sensitivity the greater is the likelihood that multiple secondary sensitizations will occur.[10] Is often-repeated exposure to the primary allergen likely to widen the pattern of cross-sensitizations? Some years ago it was suggested that repeated exposures probably tend to widen the pattern.[13] More recently, however, Fisher and associates[17] retested patients with paraphenylenediamine hypersensitivity with a small number of secondary allergens 3 to 10 years after they were first tested with the same allergens. They came to the conclusion that repeated exposure to the primary allergen does not produce additional cross-sensitizations. Furthermore, they found that repeated exposure to compounds which are immunochemically related to the primary allergen does not produce additional cross-sensitizations to these compounds. From these findings one would have to conclude, then, that the potential pattern of cross-sensitivity is established early or even genetically and undergoes little change later on. However, this important question deserves much further investigation.

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SYSTEMIC REACTION AFTER INTRAVENOUS FIBRINOLYSIN THERAPY

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A 39-year-old man had a number of abdominal operations, including cholecystectomy and subtotal gastrectomy. During his most recent period of hospitalization he suffered an ileofemoral thrombosis and was treated by intravenous injection of 100 mg. of heparin and 200,000 units of fibrinolysin. Fever and shock appeared within 3 hours after the injection, but all tenderness disappeared from the patient's ileofemoral region in approximately 10 hours. Recovery from the thrombosis and from the side-effects of the treatment was complete within three days. Immunological studies led to the hypothesis that the patient's circulation carried antibodies for streptokinase and fibrinolysin. It is suggested that fibrinolysin be used with caution until its mode of action is better understood.

Intravenous streptokinase therapy is associated with systemic reactions manifested by fever, chills, and hypotension. Impurities in the streptokinase preparation, reaction between streptokinase-inhibitor activity in the patient's blood, or reaction to the breakdown products of proteins resulting from the fibrinolytic activity of the injected streptokinase have been suggested as possible mechanisms for these reactions, which have occurred despite purification of various streptokinase preparations.[1]

Advances in the preparation of human fibrinolysin have made available a new thrombolytic agent which is effective in animals. Preliminary clinical reports have suggested that fibrinolysin is useful in the treatment of various types of acute thrombotic episodes.[2] Minor toxic reactions, such as fever and rare episodes of skin rash, have been reported with intravenous injections of human fibrinolysin.

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This report presents the case of a patient who had a severe systemic reaction after the first intravenous administration of human fibrinolysin. The profibrinolysin used in this study was purified from human plasma fraction 3. It is activated to fibrinolysin (Actase) with small amounts of purified streptokinase or urokinase, lyophilized and stored at –20 C until use. The activity is determined by in vitro assay of a purified fibrin clot by the commercial source. Bovine fibrinolysin was activated with chloroform by the manufacturer.

Table 1.—*Change in Coagulation Parameters After Intravenous Infusion of Fibrinolysin*

	Control	Immediately After Infusion	20 Hr. After Infusion
Clotting time, min.	9	10½	22
Prothrombin time, sec.	15	15	17
Prothrombin consumption, %	95	84	81
Two-stage prothrombin level, units ...	395	378	251
Fibrinogen level, mg. %	533	437	530
Whole blood lysis time at 37 C, hr.	24	24	24
Arginine methyl ester assay for fibrinolytic activity, units per ml. of plasma	3.33	3.33	5.96

Prothrombin time and two-stage prothrombin determination were performed by established methods.[3] Fibrinogen concentration was determined by the biuret method on the isolated plasma clot. Fibrinolytic activity was determined by the synthetic substrate method of Sherry and Alkjaersig,[4] with use of arginine methyl ester (TAMe). Clot lysis was determined on whole blood clots at 37 C. Platelet (direct) and white blood cell counts were determined by standard methods. Special immunological studies will be described fully later.

Report of a Case

A 39-year-old man was admitted to Jackson Memorial Hospital on July 25, 1958, because of a history of diarrhea with black-colored stools. There was a history of excessive alcoholic intake daily during the past 20 years. In 1946 a subtotal gastrectomy was performed because of a bleeding duodenal ulcer. In 1949 a cholecystectomy was performed at another hospital. In 1952 the patient was admitted to this hospital because of gastrointestinal bleeding and a vagotomy was performed. Since this last surgical procedure the patient has had no recurrence of ulcer pain. The patient was admitted to this hospital in 1953 and 1956 because of nausea, vomiting, and diarrhea, which responded to conservative treatment. A liver biopsy was performed during the admission in 1956, and diagnosis on pathological examination of the tissue was Laennec's cirrhosis. The remainder of the history is noncontributory.

Physical examination revealed blood pressure to be 120/75 mm. Hg and pulse rate 72 per minute. Head and neck findings were within normal limits. There were no spider angiomas noted on the patient's body. The lungs were clear to percussion, with scattered wheezes heard over both lung fields posteriorly. The heart was within the midclavicular line in the fifth intercostal space, with a regular sinus rhythm, and no murmurs were heard. There were numerous well-healed surgical scars over the patient's abdomen. The liver was palpable 5 cm. below the costovertebral margin and was firm, and there was a palpable spleen tip descending just below the left costal margin. Laboratory studies revealed hemoglobin level 12.6 Gm. per 100 cc., hematocrit value varying between 39 and 44%, and white blood cell count 4,900 per cubic millimeter, with a normal differential. Total serum bilirubin level was 2.4 mg. per 100 cc. and later fell to 0.95. Thymol turbidity was 4 units; alkaline phosphatase level on admission was 10.7 units and during the hospital stay fell to 6.4. Total protein level was 6.9 Gm. per 100 cc., with 4.1 Gm. of albumin and 2.8 Gm. of globulin. X-ray examination of the gastrointestinal tract and esophagus revealed no evidence of abnormality other than the subtotal gastrectomy which had been performed previously. Chest x-ray revealed an absent rib–the left eighth thoracic rib–and there was blurring of the left costovertebral angle. The patient's hospital course was unremarkable except for the persistent diarrhea, which consisted of soft, watery, light-brown stools and was negative for occult blood, parasites, and pus cells.

Table 2.—*Results of Immunological Studies with Patient's Blood*

Serum	Streptokinase-Streptodornase (Varidase)	Streptokinase-Activated Human Fibrinolysin (Actase)	Chloroform-Activated Bovine Fibrinolysin	Urokinase-Activated Human Fibrinolysin
Patient's	+	+	+	+
Rabbit antiglobulin* ...	–	+	+	+
Normal human	–	–	–	–

* Produced by repeated intramuscular injections of human fibrinolysin into rabbit. Precipitin test is carried out as follows: 0.2 ml. of serum is slowly added to 0.5 ml. of 1% solution of streptokinase or fibrinolysin. A precipitate at the junction of the two solutions indicates a positive result.

On Aug. 7, 1958, the patient had a sudden onset of severe pain in the left inguinal area while walking to the bathroom at 2 a. m. The pain became severe during the day, and examination revealed marked tenderness with some swelling in the left inguinal area. A clinical diagnosis of an ileofemoral thrombosis was made, and the patient was treated with 100 mg. of heparin and given 200,000 units of fibrinolysin intravenously over a 15-minute period. The fibrinolysin was dissolved in 200 cc. of a 5% solution of dextrose and water. Three hours after the injection of fibrinolysin the patient was noted to have a severe systemic reaction, characterized by a temperature of 104 F (40 C), pulse rate 100 per minute, and blood pressure 70/50 mm. Hg.

The foot of the bed was elevated and blood pressure maintained at a level of 110/80 mm. Hg with intravenous administration of levarterenol (Levophed) during the next 10 hours. The levarterenol therapy was discontinued; however, the patient's blood pressure again fell to 80/60 mm. Hg, and at this time he was noted to have some angioneurotic edema and slight mental confusion. The patient was treated with intravenously given cortisone, 100 mg., and levarterenol was withdrawn slowly during the next six hours. All tenderness disappeared from the patient's ileofemoral region approximately 10 hours after the intravenous injection of fibrinolysin. The next day all medication was discontinued; the patient's blood pressure was maintained at 110/70 mm. Hg. The remainder of the patient's hospital course was essentially unremarkable, and he was discharged three days later, asymptomatic.

Results of Special Blood Study.—Coagulation studies were performed on the patient's blood and are presented in table 1. There is an appreciable change in results of the various tests performed. The change in the clotting time was related to the heparin administration. The patient's plasma demonstrated an increased fibrinolytic activity 20 hours after the intravenous injection of fibrinolysin.

Special immunological studies with the patient's blood demonstrated the presence of antibodies against both streptokinase and the human fibrinolysin preparation used in the treatment of the patient. In addition, the patient's serum gave a positive result to bovine fibrinolysin and urokinase-activated human fibrinolysin (table 2).

Comment

Preliminary reports on the intravenous administration of human fibrinolysin have shown only minor toxic reactions after subsequent repeated injections.[2] In contrast, this report illustrates a severe reaction which developed in a patient after the first intravenous administration of purified human fibrinolysin, and to my knowledge this is the most severe reaction that has been observed with human fibrinolysin. The exact mechanism of this reaction is unknown. However, it may be postulated that the reaction was due to one or more of the following factors: 1. A reaction between the antistreptokinase activity in the patient's blood and the residual streptokinase protein moiety which remains in this preparation of human fibrinolysin may have occurred. This possibility seems likely since a high level of antistreptokinase activity in this patient's blood could be demonstrated. 2. The patient may have had a high antifibrinolysin titer which caused a reaction. Activity against fibrinolysin was likely because in vitro tests of the patient's serum revealed an increased antifibrinolysin titer against bovine and human fibrinolysin. 3. A systemic reaction secondary to breakdown products of the fibrinolysin-fibrin reaction may have occurred. Further studies will be necessary to establish the importance of these possible causes, since no definite conclusions can be drawn from this single case. This report does serve one useful purpose: it illustrates that a severe systemic reaction can occur with rapid infusion of fibrinolysin and suggests that this agent should be used with caution until further clinical evaluation has demonstrated the mechanism of the systemic reaction illustrated in this report.

Summary

A case of a severe systemic reaction after the first intravenous injection of purified human fibrinolysin occurred in a patient with an acute ileofemoral vein thrombosis. Immunological studies suggested that both streptokinase and fibrinolysin antibodies were responsible for the reaction observed.

4701 N. Meridian Ave. (40).

The bovine fibrinolysin used in this study was supplied through Dr. E. C. Loomis, Parke, Davis & Company, Detroit. The human fibrinolysin used in this study was supplied through Drs. R. V. Chappie and H. O. Singher, Ortho Research Foundation, Raritan, N. J.

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GLOVE POWDER GRANULOMA IN PERITONEAL CAVITY

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Six weeks after a laparotomy for duodenal ulcers a patient returned to the hospital with findings strongly suggesting acute appendicitis. When the peritoneal cavity was reopened, approximately a liter of fluid was found, and the terminal ileum, cecum, and ascending colon were studded with innumerable vesicular lesions, 2 to 3 mm. in diameter, each containing a minute white center. The condition had an appearance of a granulomatous enteritis not amenable to surgery, and correction was not attempted. Persistent symptoms and radiologic abnormalities necessitated reoperation two weeks later, when resection of the terminal ileum, cecum, and ascending colon, with ileocolostomy, was carried out. Microscopic examination of the tissues indicated that the small lesions were starch granulomas. It appeared likely that a minute quantity of glove powder from the first operation had sufficed to cause this severe reaction leading to serious diagnostic problems and a long period of disability.

Starch-derivative glove powder, when deposited in wounds or on serosal surfaces, even in minute quantities, may produce serious local foreign-body reaction. Fortunately, clinical evidence of starch granuloma is infrequently observed, as indicated by the relative sparsity of pertinent reports in the literature. When it is encountered, therefore, the etiology may be unsuspected, and it may be extremely difficult to assess. A case report illustrating this point follows.

Report of a Case

A 39-year-old man underwent laparotomy for persistent duodenal ulceration on Oct. 4, 1957. Convalescence was uncomplicated until Nov. 18, 1957, when he reported that he had had right lower quadrant abdominal pain and slight rectal bleeding for the preceding week.

Examination of the abdomen revealed only diffuse tenderness across the lower part. Proctologic examination to 15 cm. disclosed a posterior midline fissure, increased granularity and friability of the rectal mucosa, and edema and fixation at the rectosigmoid junction. On the basis of these findings, a diagnosis of extracolonic inflammatory disease was considered and hospital admission for the purpose of further study was arranged.

The patient came for admission several hours earlier than arranged and had findings strongly suggestive of acute appendicitis. Operation was promptly carried out, and when the peritoneal cavity was entered approximately a liter of free fluid was encountered. The terminal ileum, cecum, and ascending colon were studded with a myriad of tiny vesicular lesions, 2 to 3 mm. in diameter, each containing a minute white center. Many of these lesions had apparently broken down to produce shallow serosal ulcers (fig. 1), much like the common aphthous ulcer occurring on buccal surfaces. The cecum was rather markedly indurated, as were the fat appendages of the colon and the tail of the omentum, while the pelvic peritoneum was the site of milder inflammation. It was felt that these findings explained the proctologic picture.

Histological examination of fat tags revealed mild inflammation and fat necrosis. Believing that we were dealing with some unusual type of granulomatous enteritis and being uncertain of the fitness of the transverse colonic mucosa for primary anastomosis, we considered further intervention to be unwise.

On Dec. 2, 1957, x-rays of the colon were reported as showing gross deformity and filling defect of the cecum and a diagnosis of carcinoma of the cecum was suggested by the radiologist. The mucosal pattern of the transverse colon appeared to be normal. On Dec. 4, a resection of the terminal ileum, cecum, and ascending colon, with primary ileotransverse colon anastomosis, was carried out.

Histological study of the specimen revealed foreign-body reaction with granulomas, the giant cells of which contained refractile particles (fig. 2). No malignant disease was present. Chemical analysis of the tissue was reported as negative for silicon and starch, but additional microscopic examination revealed that the particles displayed the staining characteristics of starch and, when viewed with polarized light, exhibited the Maltese cross (fig. 3).

Because of persistent abdominal discomfort, this patient was unable to return to his regular work for a full year.

Comment

Since 1947, when Lee and Lehman[1] reported their experimentation with substitutes for talc as a glove lubricant, talc has been almost completely displaced by starch-derivative powders. While the hazards associated with the use of talc have been well known, it appears that the irritant properties of starch have been overlooked by most surgeons.

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In 1952, Graham and Jenkins[2] discussed the relative merits of talc and starch as glove lubricants and indicated that, although vastly superior to talc in biological properties, starch powder is by no means harmless. Also in 1952, Lee and associates[3] made a comprehensive study of the biological properties of starch-derivative glove powders and pointed out some of the factors which may influence the morbidity resulting from implantation of these agents. Wise[4] described unfavorable reactions of the brain and spinal cord to starch powder, and Sneierson and Woo[5] described complications of implantation of starch in surgical wounds in two cases. McAdams[6] reported three cases of starch powder granuloma occurring after operation and stated that starch granules are identified daily on surgical specimens sent to the pathology laboratory.

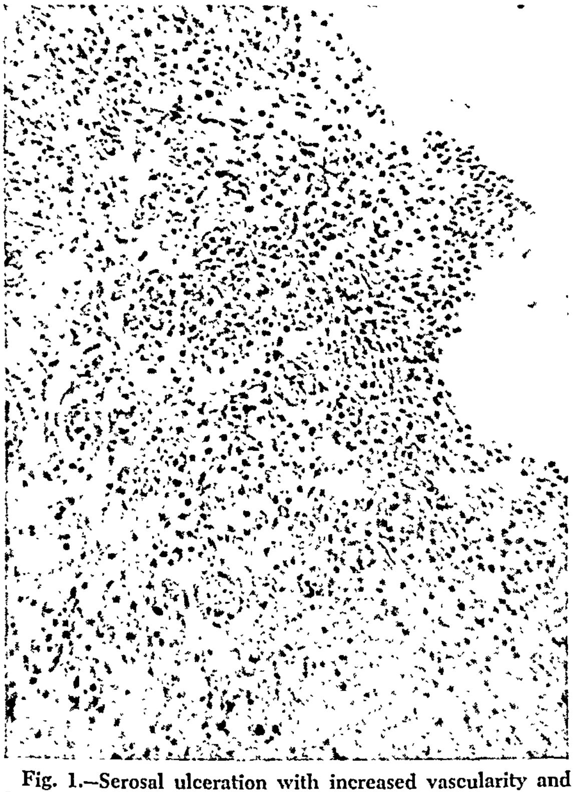

Fig. 1.—Serosal ulceration with increased vascularity and dense collection of inflammatory cells in base of ulcer (100 ×).

Undoubtedly, deposition of starch powder on wound surfaces and viscera occurs much more frequently than suspected. It has been clearly shown that this material is absorbed in the tissues in most cases, but it does produce local foreign-body reaction as long as it remains unabsorbed.[3]

In our case, a minute quantity of starch was sufficient to produce a severe reaction leading to serious diagnostic problems and a long period of disability. In retrospect it is seen that if the correct diagnosis had been made at the time of the second operation subsequent operative procedures could

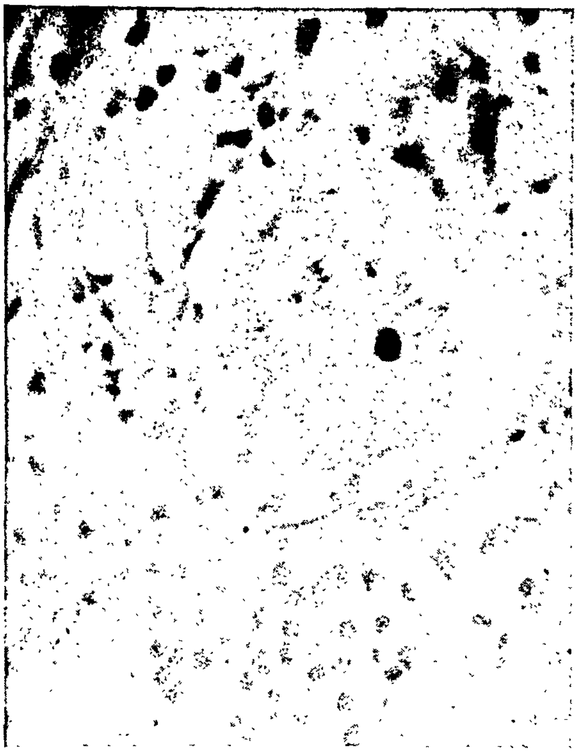

Fig. 2.—Foreign body giant cell containing starch granule stained with Feulgen's stain (440 ×).

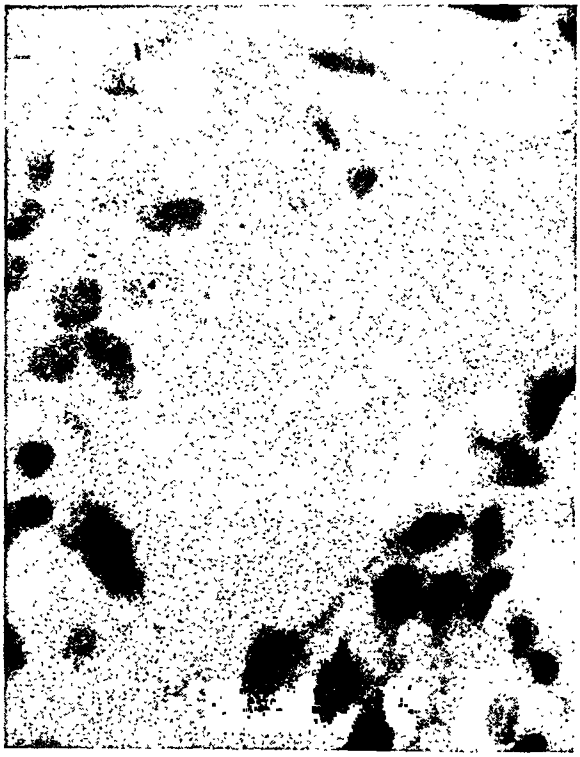

Fig. 3.—Foreign body giant cell containing starch granule, viewed with polarized light; Maltese cross is characteristic of starch (950 ×).

have been avoided. This could have been accomplished by examination of multiple biopsy specimens with polarized light, had we been aware of the fact that starch may produce such lesions. In the future, any questionable reaction observed during reexploration will be investigated in that manner.

Starch granules may be seen as refractile particles in giant cells. They may be identified positively by their reaction to iodine and the appearance in the granule of the characteristic Maltese cross when viewed with polarized light.

Scrupulous preoperative lavage of gloves and other latex articles should be mandatory. Basins and water used for this purpose should be discarded promptly in order to avoid transfer of starch powder to the wound. Glove changes with the attendant dust cloud should be effected at a safe distance from the operating table to avoid fall-out in the wound.

Summary and Conclusions

A case of starch granuloma presented serious diagnostic problems and produced long-term disability.

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CLINICAL NOTES

THE MANAGEMENT OF CARDIAC ARREST

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No emergency demands more immediate surgical intervention for the preservation of the life of a patient than that which attends cardiac arrest in the operating room. If more than a few minutes lapse between the time of cessation of the heartbeat and restimulation of the heart by massage and electricity, one of three things will inevitably result: 1. The patient will die on the operating table. 2. The heartbeat may be restored, even after the maximum length of time for obtaining a satisfactory end-result, but the patient will die within a few hours or a day or two at the most. 3. The most tragic end-result is to be found when the heartbeat has been restored after too long a delay and the patient survives indefinitely without any intelligence.

For a patient to live weeks, months, or even years with the brain cells thus severely damaged by prolonged anoxia is more dreadful to contemplate than death itself. Every surgeon should be alert to the possibility of facing this critical situation whenever an anesthetic is being given and an operation is being performed on his patient.

The patient was a 17-year-old male. The operation was supervised by a senior attending orthopedic surgeon who was not surgically prepared to assist in the operation. The end-result in this case was not one of tragedy, but the tenseness of the few moments during which the life of the patient was dependent on the alertness and quick performance of the team of young resident surgeons constituted a lesson which had a real impact on the resident staff and on some of the attending surgeons who were aware of what had happened.

Those skeptics who blithely decide that "it can't happen to me" should recognize that cardiac arrest can happen to the patient of any surgeon during any operation. Action, in the event of a cardiac arrest, should be anticipated and should be planned before one starts any operation and before one enters the operating room.

Treatment of a patient with a severe or progressive scoliosis, which is uncompensated, requires maximal correction with a Risser turnbuckle or localizer cast. After maximal correction of the deformity has been obtained, it has been customary in many orthopedic clinics to perform the surgical fusion of the spine through a window in the back of the cast which is left on to maintain correction during and after the operation. In addition to presenting the procedures which were utilized to save the life of the patient in the case presented here, we wish to express condemnation of the practice of

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operating on patients who are in a body cast, unless the cast has been bivalved prior to start of the anesthesia.

Report of a Case

A 17-year-old male entered Chicago Wesley Memorial Hospital after examination in the orthopedic clinic of Northwestern University Medical School and after consultations at the weekly clinical conference of the orthopedic department of the hospital. Idiopathic scoliosis of the spine was marked. The deformity was severe, and there was no compensatory or secondary curve to balance the primary curve. The patient complained of pain in the lower thoracic vertebrae.

For two months Risser localizer casts were used to obtain as much correction as possible. A 60-degree primary curve was reduced to one of 30 degrees. When it was thought that a maximal correction had been obtained, the first of a two-stage spine fusion was scheduled. Segments T-5 through T-9 were fused without any complications. This first-stage fusion was done after complete removal of the cast. Two weeks after the first-stage operation, another cast was applied, extending from the groin to and including the shoulders. One week later, on April 18, 1957, the second stage of the spinal fusion was scheduled and this was planned to be carried out through a window in the cast.

All operations at Chicago Wesley Memorial Hospital in which the patient is placed in the prone position on the operating table are carried out with use of endotracheal anesthesia. Intubation of this patient was uneventful. There was, however, some immediate difficulty in obtaining a good respiratory exchange. Not until the patient was breathing freely and easily through the intubation tube was he turned onto his abdomen.

Immediately after the skin incision was made it was noted that the blood was abnormally dark. This was brought to the attention of the anesthesiologist. The respiratory exchange became more labored and less satisfactory. Approximately five minutes later the skin incision was closed. The anesthetist reported that the pulse was feeble, the blood pressure had dropped, and the unsatisfactory condition of the patient was continuing in spite of the administration of vasopressin.

At 9:47 a. m., 45 minutes after anesthetization was started, the pulse could not be felt and no blood pressure recording could be obtained. The patient was immediately turned over and the body cast was cut in the midline and turned back. With the cast still in place, but spread widely to expose the anterior portion of the thorax and abdomen, the thorax was opened in the fifth interspace on the left side; cardiac massage was started at 9:48 a. m., one minute after the anesthetist had reported no pulse and no demonstrable blood pressure. The resident surgeon (P. H. D.) noted immediately that the heart was in ventricular fibrillation. The pericardial sac was opened and the heart delivered through the defect. A slow drip of 1% solution of lidocaine (Xylocaine) hydrochloride was started over the myocardium. The defibrillator was then used three times before a regular rhythm was established at 10:17 a. m. The patient was digitalized during this procedure, and adequate exchange of oxygen was maintained.

The thoracic cavity was left open in order to observe the heart action during the time in which the cast was removed from beneath the patient and the skin surgically prepared and draped. One million cubic centimeters of penicillin was instilled into the pericardial sac and into the wound about the pericardium. Two rubber thoracotomy tubes were inserted, and the incision was closed.

By 11:30 a. m., the patient had regained consciousness and was answering questions. His subsequent recovery was uneventful. The thoracotomy tubes were removed in 48 hours and the sutures in 10 days. There was no wound infection in spite of the dirt and plaster dust which was present on the skin in the area of the incision at the time that the chest was opened.

This patient was discharged 18 days after operation and has been seen at regular intervals since that time. He has noted no change in his ability to think and remembers events immediately before and after the operation. Six months after the operation, he had returned to school and was making good grades.

The foresight of the orthopedic and of the surgical resident in having immediately available on an adjoining table a motor-driven cast saw, and the fact that the cast was relatively thin, made it possible to remove the cast from over the chest within a matter of seconds. As a result of this experience, the practice of operating through any window in a cast has been discouraged at Chicago Wesley Memorial Hospital. Patients who have been treated by localizer casts may be operated on lying in the anterior half of the cast. About two weeks after the operation, a new cast, with use of the localizer technique to obtain additional correction, if possible, should be applied.

This patient had no difficulty in breathing prior to going to the operating room, and the inadequate air exchange that followed the introduction of an intratracheal tube was completely cleared up, so that there was a good respiratory exchange for some minutes before the patient was turned over to prone position to prepare the back for the operation. There was nothing in the preoperative history which might have caused anyone to suspect that there might be a near tragedy such as has been described. The experience gained from this case has alerted all of the house staff and most of the attending surgical staff of the hospital so that they will be prepared for immediate intervention in the event that another episode of cardiac arrest does occur at some time in the future, as it is most certain to do in any operating room where a large number of operations are being carried out week after week.

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CLINICAL USE OF PHENISTIX REAGENT STRIP METHOD OF TESTING URINE SAMPLES

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In 1934 Følling described phenylpyruvic oligophrenia and the characteristic color reaction of the urine with ferric chloride.[1] Since then the disease has been related to a hereditary deficiency of the enzyme which converts phenylalanine to tyrosine, and lately it has been shown that the earlier in life a diet low in phenylalanine is instituted, the better the chances for ameliorating the convulsive, behavioral, and intellectual disturbances of this disorder.[2] Hence the ferric chloride test, already widely used in the diagnostic evaluation of mental deficiency, has assumed practical importance. Recently the usefulness of a simple and reliable paper strip method (Phenistix reagent strips) of detecting phenylketonuria has been reported.[3]

The present note deals with the use of an improved form of Phenistix. The test material consists of a stiff strip of cellulose impregnated with ferric and magnesium ions and cyclohexylsulfamic acid. The ferric ions react with phenylpyruvate to give a gray to blue color proportionate to the amount of phenylpyruvate present; the magnesium ions minimize interference by urinary phosphates, while optimal color reaction is facilitated by the cyclohexylsulfamic acid buffer. The strip is dipped into the urine sample or saturated by pressing against a wet sheet or diaper. The test sample should be as fresh as possible. Color reaction occurs within a few seconds. A final reading is made at 30 seconds and the color compared with the scale provided with the Phenistix.[4]

Urine samples from 35 patients with known phenylketonuria institutionalized at the Fernald, Myles Standish, and Wrentham state schools of Massachusetts and the Massachusetts General Hospital were tested by both the paper strip method and, after acidification, with 10% ferric chloride solution. Also tested by both methods were cotton balls wet with 5 drops of the urine sample. In each instance the paper strip method gave a reaction at least as intense as that given by ferric chloride. Furthermore, the paper strips held their color longer, whereas the mildly positive solution color faded rapidly at warm room temperatures. To insure the reaction when testing the cotton balls, the paper strips had to be pressed against them and be allowed to soak up the urine. Ten urine specimens, retested after standing in the refrigerator at 40 F for three weeks, reacted as previously with Phenistix, but gave weaker reactions with the solution.[5]

In one child being treated with a low phenylalanine diet, the parents were able to follow the regression of phenylketonuria by the use of the paper strips, while serum phenylalanine levels were obtained periodically. Phenistix still gave a faintly positive reaction at a time when the serum phenylalanine level was only 3.5 mg. % (about twice normal), whereas the ferric chloride solution test on the same urine sample was negative.

Other Uses for Test

Ferric chloride solution added by drops to boiled urine of patients who have ingested large amounts of salicylates results in a characteristic purple color reaction. The urine samples of children receiving therapeutic amounts of acetylsalicylic acid for rheumatic fever or rheumatoid arthritis, or admitted for salicylism, were tested with the paper strips as well as the ferric chloride solution. Purple reactions were observed in all.

Similarly, Fellman[6] and Pollack[7] have reported that urine samples of patients receiving phenothiazine derivatives give a purple reaction with ferric chloride solution. In testing the urine samples of 12 patients from the Lemuel Shattuck Hospital, Boston, who were receiving treatment with various tranquilizers, those of 5 receiving prochlorperazine (Compazine) and 5 receiving chlorpromazine (Thorazine) gave a light to deep purple reaction with Phenistix as well as with ferric chloride solution; the tests of urine samples of 2 patients receiving meprobamate gave negative results by both methods.

The depth of the color reaction by both methods with salicylate and phenothiazine metabolites reflects the amounts of the respective drugs excreted by the patients. While the purple reaction to salicylate metabolites has more of a bluish hue compared to the more reddish one with the phenothiazine derivatives, the colors obtained were always clearly distinguishable from the gray to blue reaction of Phenistix or green-blue of ferric chloride solution with phenylpyruvic acid.

Conclusions

Phenistix appears to have a dual usefulness to physicians. It provides a convenient method for the repeated testing of urine samples of all infants in the first few months of life to detect those with phenylketonuria and for following those being treated with a diet low in phenylalanine, and also it offers a simple means for screening patients suspected of intoxication due to salicylates or phenothiazine derivatives.

Fruit Street (14).

The reagent strips used in this study were supplied as Phenistix by Ames Company, Inc., Elkhart, Ind.

Chief Resident, Children's Medical Service, Massachusetts General Hospital, and Teaching Fellow, Harvard Medical School.

Urine specimens from patients with phenylketonuria and from those receiving tranquilizers were made available through Drs. C. V. Pryles, R. Cooke, K. V. Quinn, and T. C. Hall from the Fernald, Myles Standish, and Wrentham state schools of Massachusetts and the Lemuel Shattuck Hospital respectively.

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CARDIAC ARREST OCCURRING OUTSIDE THE OPERATING ROOM

DEMONSTRATION OF EFFECTIVENESS OF A TRAINED RESUSCITATION TEAM

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Successful resuscitation of patients who develop cardiac arrest in the operating room has become almost commonplace in current medical practice. Many hospitals train their operating room personnel in the necessary emergency principles and techniques of treating this complication. Theoretically it is possible to resuscitate patients who develop cardiac arrest outside the operating room if the proper conditions prevail. Since the cerebral cortex can withstand only three to four minutes of anoxia before irreversible damage occurs, the primary condition for successful treatment must be that personnel and equipment should be at hand at the time of the emergency.

The Newark (N. J.) Beth Israel Hospital cardiac arrest team has been organized to assure that immediate therapy can be instituted anywhere within the hospital. This has been accomplished by training programs, the establishment of a house staff resuscitation team, and the judicious placement of emergency equipment.[1] Partly as a result of this program, a successful outcome was achieved in the following case of cardiac arrest that occurred in a hospital ward.

Report of a Case

A 53-year-old man was admitted for the first time to the Newark Beth Israel Hospital on April 26, 1958, complaining of severe upper abdominal pain of one day's duration. The pain was associated with a mild fever, moderate constipation for two days, and urinary frequency. There were no other significant complaints. There was a history of treatment two and five years prior to admission for "stomach ulcer." Further details were unavailable.

Pertinent physical findings were limited to the abdomen where there was generalized spasticity and tenderness of the right upper abdomen. His blood pressure was 130/80 mm. Hg; pulse rate was 90 per minute; heart sounds were normal, with aortic second sound greater than pulmonic second sound, with no thrills or murmurs.

Laboratory data, including a complete blood cell count, fasting blood sugar level, and blood urea nitrogen level, were within normal limits. X-ray studies of the gallbladder and kidneys revealed no abnormality. An upper gastrointestinal series demonstrated a pyloric ulcer.

Clinical Course.—Shortly after admission the patient became asymptomatic. On May 9, 1958, an exploratory laparotomy was performed. Premedication was attained with 100 mg. of meperidine hydrochloride and 0.4 mg. of atropine sulfate. Anesthesia was induced with thiopental sodium and succinylcholine chloride, both given intravenously, and nitrous oxide-oxygen given endotracheally. A 75% subtotal gastrectomy was performed for a penetrating prepyloric ulcer. An anterior isoperistaltic Hofmeister gastroenterostomy was performed. The appendix was removed. At the close of the uneventful operation the patient was in good condition, with a blood pressure of 130/80 mm. Hg and a pulse rate of 96 per minute.

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Shortly after return of the patient to his ward bed, the nurse noted that he was cyanotic and pulseless. She immediately paged the anesthetist and the intern and, while waiting for their arrival, brought the emergency cardiac instruments to the bedside. Both the anesthesiologist, Dr. William Evers, and the intern, Dr. Michael Levy, arrived at the scene within a minute. On confirming the diagnosis of death, Dr. Evers opened the chest through the left fifth intercostal space with the scalpel that the nurse had ready for him. There was no bleeding from the incision. The heart was found to be dilated and at standstill.

The intern gave mouth-to-mouth respiration. After several manual compressions, a regular rhythm resumed and brisk bleeding from the intercostal arteries was noted. While the intern maintained intermittent cardiac compression and the anesthetist continued the mouth-to-mouth respirations, the patient was wheeled on a stretcher through the hospital corridors to the operating room. An endotracheal tube was passed and the patient oxygenated. A blood transfusion was started. The bleeding from the intercostal arteries was controlled, the thoracic incision closed, and a thoracotomy tube placed on constant suction.

Table 1.—*Reported Cases in Literature of Cardiac Arrest Outside Operating Room*

Author	Room Where First Treatment Given	Therapy*	Original Heart Status†	Etiology	Complications	Known Survival
Reagen, L B, and others. Surgery 39:482, 1956	Hospital	Endo O_2, M, S	VF	Myocardial infarct	...	4 yr.
Beck, C S., and others: J A. M. A 161:434, 1956	Emergency	M; Endo O_2; S, 5 times	VF	Myocardial infarct	...	2 yr.
Mozen, H. E., and others: J. A M. A. 162:111, 1956	Hospital	M, m-m O_2, S	VF	Rheumatic heart disease	...	5 wk.
Celio, A.: J. Internat Coll. Surgeons 25:299, 1956	Hospital	M; S, 3 times	VF	Myocardial infarct	...	4 mo.
Brown, C. D., and others: J. A. M. A. 163:352, 1957	X-ray dark room	M, Endo O_2, KCl	St-VF	Wolff-Parkinson-White syndrome	Empyema	22 mo.
Belshe, J. C.: Personal communication to authors	Emergency	M, Endo O_2	St	?	...	1½ yr.
Bloomfield, D. K., and Mannick, J. A. New England J. Med. 258:1244, 1958	Hospital	M, S	VF	Myocardial infarct	Empyema	1 mo.
Ibid.	Hospital	M, S	St-VF	Myocardial infarct	Transient hemiparesis	3 mo.
Schwartz, A. M., and Lobell, S. M.: J. A. M. A. 166:488, 1958	Hospital	M, m-m O_2, Endo O_2, S	St-VF	Sulfobromophthalein reaction	...	7 mo.
Williams, G. R., Jr., and Spencer, F C: Ann Surg. 148:462, 1958	Emergency	Endo O_2	St	Asthma	...	2 mo.
Ibid	Hospital	M	St	Pneumothorax from ice pick wounds	Permanent visual defect	2 mo.
Ibid.	Emergency	Endo O_2, M	St	Cardiac tamponade from knife wound	...	1 mo.
Zoll, P. M., and others: New England J. Med. 254:541, 1956	Hospital	Pacemaker	St	During pericardiocentesis	?	?
Douglas, A. H., cited by Zoll, P. M., and others: New England J. Med. 254:541, 1956	Hospital	Pacemaker	St	Myocardial infarct after 200 mg. procainamide	?	?
Present study	Hospital	M, m-m O_2, Endo O_2	St	Postoperative	Empyema, pericarditis	7 mo

*M—transthoracic cardiac massage; S—electric shock; Endo O_2—Endotracheal oxygen; m-m O_2—mouth-to-mouth respiration.
† VF—ventricular fibrillation; St—standstill.

Within five minutes of the cardiac massage, spontaneous respirations returned, the blood pressure was 110/70 mm. Hg, and the pulse rate was regular at 120 to 130 per minute. Both pupils were equal, constricted, and reacted to light. The patient was moving about and indicated with his hand that he had pain in his abdominal incision. Nevertheless the endotracheal tube was left in place for two hours, at which time his blood pressure rose to 140/90 mm. Hg and his pulse rate remained at 130. After removal of the endotracheal tube, the patient was fully conscious and talking; his general condition appeared satisfactory. Oxygen therapy was continued by intranasal catheter. A unit of salt-free albumin was given intravenously. An electrocardiogram showed a regular sinus tachycardia with no evidence of myocardial damage. After three hours the patient was returned to his room in relatively good condition.

As far as his abdominal surgery was concerned, the patient made an uneventful recovery. However, his postoperative course was complicated by the development of empyema on the left side and acute pericarditis due to hemolytic Staphylococcus aureus. He remained acutely ill with this complication for six weeks. During his convalescent period he was treated with numerous antibiotics, including chloramphenicol, novobiocin, sulfamethoxypyridazine, ristocetin, penicillin, streptomycin, and sodium sulfathiazine. Chlorpactin W C S-90 (stabilized, buffered, organic hypochlorous acid derivative) irrigations were also used.

His postoperative course was further complicated by a prerenal azotemia, hypoproteinemia, and a toxic psychosis. At the height of his illness he developed auricular fibrillation and congestive heart failure that responded to digitalization. Improvement was gradual, but he was ready for discharge on July 19, 1958. A discharge reevaluation of his condition was as follows: He was afebrile, with normal pulse, blood pressure, and respirations. The heart sounds were of good quality; no murmurs were heard. The rhythm was regular sinus. The blood pressure was 125/70 mm. Hg. An electrocardiogram revealed inverted T waves in standard leads 1, 2, 3, and V_2 through V_6. These changes were interpreted as residuals of the suppurative pericarditis. The chest x-ray revealed a residual patch of fibrosis at the base of the left lung. Clinically there was no impairment of pulmonary function. Blood chemistry tests were performed and were all within normal limits except for a total protein value which revealed a reversal of the albumin-globulin ratio (albumin 3.5, globulin 4.3 Gm. per 100 cc.). Six months postoperatively the patient was clinically well.

Comment

Through the heroic efforts of the anesthetist and the intern, this patient is now well. However, were it not for the fact that the proper equipment was at hand, the outcome might not have been so fortunate. Each nurses' station is equipped with a sterile scalpel hung in an accessible spot and labeled appropriately. We believe that this is the only instrument necessary to initiate therapy. An emergency call on the hospital loudspeaker system summons the members of the cardiac arrest team, who bring additional material. Essentially, this consists of appropriate surgical instruments and drapes, laryngoscopes and endotracheal tubes, various drugs, a cardiac pacemaker, and an electrocardiograph.[1]

In table 1 are listed successful cases of treatment of cardiac arrest occurring outside the operating room as reported by others. These clearly indicate that such resuscitative measures have some practical importance. We believe that it is pertinent to report all such experiences so that some criteria can be established to determine proper circumstances for undertaking emergency resuscitative measures. Delineation of policy is also important from a medical-legal standpoint. At present it is not clear whether a physician would be held liable for assault and battery (or, perhaps, manslaughter) if therapy failed, or for malpractice if therapy was not attempted.

At the Newark Beth Israel Hospital, we have established, tentatively, the following set of principles necessary for the success of this approach: 1. A physician must be present or in the immediate vicinity at the moment of cardiac arrest. 2. "Cardiac arrest" must be the primary diagnosis. 3. At least two, but preferably three, physicians must confirm the diagnosis of death and agree to the proposed therapy. 4. The cardiac arrest team must be summoned to participate in the emergency care. Treatment must not be delayed by waiting for the entire team to assemble. 5. Treatment must be started within three to four minutes. We believe that these recommendations provide the treating physicians adequate emotional and legal protection to allow them to treat the emergency. In this way, no single individual will carry the entire responsibility.

It might appear that time would be lost in adhering to the above principles. However, in actual practice, most of the decisions can be reached in short order. We have demonstrated repeatedly in practice drills that at least eight members of the cardiac arrest team will arrive within two minutes of the emergency call. Enough time remains, therefore, to reach a decision and institute indicated resuscitative measures.

In the past two years we have demonstrated to our satisfaction the efficacy of our program in the treatment of cardiac arrest occurring in the operating room. As can be seen in table 2, there has been a marked decrease in incidence and increase in survival rate in these cases. We believe that the use of a cardiac monitor-alarm on every anesthetized patient has been of great value in achieving these results. Constant monitoring of the heartbeat permits the observer to correct arrhythmias and insures instantaneous treatment in the event of cardiac arrest.

TABLE 2.—*Cardiac Arrest in Operating Room*

Yr.	Cases, No.	Survival, No.	Survival, %
1952-1955*	18	4	22
1956	9	2	22
1957	8	3†	37
1958	3‡	2	67
Total	38	11	29

* Probably does not include all cases (registry started 1955).

† Universal use of cardiac monitor instituted in October, 1957. Two of three survivors had monitors on.

‡ Monitor used in all cases.

The case presented in this report illustrates that the entire inhospital program is profitable in decreasing the death rate from cardiac arrest occurring outside the operating room. We believe that concerted efforts to treat these cases will be fruitful.

Summary

Successful resuscitation can be attributed to the prompt and decisive action taken by the physicians first to arrive at the bedside and to the training and preparation of a hospital resuscitation team. The hospital training program for the treatment and prevention of cardiac arrest and the use of a cardiac monitor-alarm on every anesthetized patient have resulted in substantial decrease in incidence and in an increase in survival in cases of cardiac arrest occurring in the operating room. The extension of this program to include cases of cardiac arrest occurring elsewhere in the hospital should prevent more cases of sudden death.

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COUNCIL ON DRUGS

Report to the Council

The Council has authorized publication of the following report. Nonproprietary terminology is used for all drugs that are mentioned; when such terminology is not considered to be generally well known, its initial appearance is supplemented by parenthetic insertion of names known to be applied to commercial preparations. H. D. Kautz, M.D., *Secretary.*

CURRENT STATUS OF THERAPY IN RHEUMATIC FEVER

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Any discussion of therapy in rheumatic fever must, of course, be concerned with the extremely important aspect of prevention as well as with treatment of the attack which has already begun. The measures of importance in prevention can be stated with confidence in the light of progress made over the past 30 years. Unfortunately, however, one can write with far less certainty about the treatment of the established attack. In this presentation, both prevention and treatment will be considered and the evidence for and against the important unsettled issues will be briefly discussed. In addition, some aspects of the treatment of patients with inactive rheumatic heart disease will be included.

Prevention

The evidence that rheumatic fever does not occur without a preceding infection due to a group A hemolytic streptococcus is now so well established that it is necessary to mention only a few of the more important recent studies in a discussion such as this. Indeed, as long as 20 years ago, almost everyone studying the disease had accepted the convincing evidence provided by the antistreptolysin-O determination, which had been repeatedly shown by Coburn and others to be high in some 85% of patients with rheumatic fever, irrespective of whether there had been a clinically apparent preceding hemolytic streptococcic infection. Nevertheless, there still were a few investigators who believed that some, at least, of the remaining 15% of cases might have other causes. Then, in 1954, Stollerman and co-workers showed that, if one used tests for not merely one but three hemolytic streptococcic antibodies, positive evidences of a recent infection by these micro-organisms could be demonstrated in approximately 99% of cases. Thus, the evidence is now overwhelming that a prior hemolytic streptococcic infection is an essential to all attacks of rheumatic fever.

The important practical application of these basic studies has been the demonstration that, by prevention of hemolytic streptococcic infections or by prompt, intensive treatment of an existing infection, rheumatic fever can, in turn, be prevented. Prevention thus can be considered under two headings, continuous prophylaxis against the start of a hemolytic streptococcic infection and intensive treatment of an infection which has begun.

Continuous Prophylaxis.—There are a number of satisfactory regimens for continuous prophylaxis. The ones which will be mentioned here are those recommended by the Council on Rheumatic Fever and Congenital Heart Disease of the American Heart Association, listed in the order of my preference: (1) benzathine penicillin G (Bicillin, Permapen), one intramuscular injection of 1,200,000 units every four weeks; (2) sulfadiazine or a preparation of multiple sulfonamides in doses of 500 mg. (for children weighing under 60 lb. [27.2 kg.]) or 1.0 Gm. (for persons weighing 60 lb. or more) daily by mouth in a single dose; or (3) penicillin in the form of a buffered soluble salt of penicillin G, sodium penicillin O (Cer-O-Cillin sodium), or *phenoxymethyl penicillin* (*Pen-Vee, V-Cillin*), 250,000 units by mouth two times daily. All these regimens are effective, but benzathine penicillin G given intramuscularly has consistently been found to give slightly greater protection than the others. This probably is due, at least in part, to the special advantage that, since the physician gives the injection himself, he can be certain that the patient is really receiving it. All too frequently when oral medication is being taken at home, doses are missed sufficiently often to permit a hemolytic streptococcic infection to break through. However, in patients who object to an injection once each month or in the occasional patient in whom local reactions occur at the site of injection severe enough to make this method inadvisable, either of the other regimens will give excellent protection if followed faithfully by the patient.

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There are two vital questions concerning continuous prophylaxis. Who should receive it, and how long should it be continued? Absolute answers cannot be given to either question at present, but the following rules are recommended. Continuous prophylaxis should be given to any child (and probably also to any patient below the age of 25 years) who has ever had an attack of rheumatic fever or who has definite heart disease of the rheumatic type, even in the absence of a history of any illness suggesting rheumatic fever. In adults, it should be given after a recent attack of rheumatic fever or if rheumatic heart disease (active or inactive) is present. It probably is not indicated merely because of a history of rheumatic fever in the remote past in an adult whose heart is normal.

The question of length of time prophylaxis should be continued is particularly difficult. In the present state of knowledge, it probably is best to start continuous therapy with the thought that it will be kept up throughout the patient's life if heart damage already exists, and at least well on into adulthood in a child with a history of rheumatic fever but with a normal heart. It can be hoped that, before many more years have passed, new information will be available which will permit a better answer to this question. Meanwhile, no rules of thumb can be established governing continuous prophylaxis which can supplant the judgment of the physician responsible for the individual patient.

Another point of importance in continuous prophylaxis is the need for higher doses given temporarily to provide added protection when procedures such as dental extractions and major or minor surgical operations are being performed which permit bacteria to enter the blood stream. Penicillin and sulfonamides in doses used for continuous prophylaxis are sufficient to prevent infections by hemolytic streptococci and other sensitive bacteria. The blood levels induced are not high enough, however, to control alpha hemolytic streptococci or other resistant micro-organisms. Hence, additional protection is indicated when there is danger that the introduction of bacteria may cause the implantation of bacterial endocarditis on heart valves already damaged by rheumatic valvulitis. The following regimen is recommended: On the day of operation, 600,000 units of an aqueous soluble penicillin G salt plus 600,000 units of procaine penicillin G (Crysticillin, Depo-Penicillin, Diurnal Penicillin, Lentopen, Procaine Penicillin G) are given by injection shortly before the operative procedure. For two days after, 500,000 units of penicillin are administered orally four times a day. For patients who cannot be given penicillin, erythromycin (Erythrocin, Erythromycin, Ilotycin) or the broad-spectrum antibiotics can be used. In patients who are to undergo surgery of the urinary or lower gastrointestinal tract, oxytetracycline (Terramycin) hydrochloride or chlortetracycline (Aureomycin) hydrochloride should be administered in full doses instead of penicillin. Similar protection should be given to patients with congenital heart disease who are to undergo any procedure likely to be associated with transient bacteremia.

Finally, it must be emphasized that the discovery of the value of continuous prophylaxis places a greater responsibility than ever on the physician for making a correct diagnosis of rheumatic fever and of rheumatic heart disease. Failure to institute protection when it is required will often result in further rheumatic attacks, with the tragic progression of cardiac damage so familiar before the era of continuous prophylaxis. On the other hand, it is no light matter to start a patient who does not need it on a course which calls for continued administration of a drug over a period of many years. In this dilemma, strict diagnostic criteria are advisable, such as the "modified Jones Criteria" obtainable through the American Heart Association. If the diagnosis is in doubt it probably is preferable not to start continuous prophylaxis but to warn the patient of the possible special hazard to him of hemolytic streptococcic infections. Then, at the first symptom of sore throat, a culture can be taken, and, if the infection proves to be due to hemolytic streptococci, intensive penicillin therapy can be given as outlined in the following section.

Penicillin Therapy.—Massell, Rammelkamp, and others have shown that intensive antibiotic therapy of a hemolytic streptococcic infection of the pharynx will prevent the subsequent development of rheumatic fever. The sooner this can be started the better, but there is good evidence that it is worth while even up to the 10th day after the start of the infection. Two points of major importance must be stressed. The first is that a bactericidal agent is required for the elimination of an existing infection, whereas a merely bacteriostatic agent like sulfadiazine is effective in continuous prophylaxis to prevent a hemolytic streptococcic infection from starting. Hence, the sulfonamides cannot be used for this purpose. The second point is equally important, namely, that an effective blood level of penicillin must be maintained at least 10 days to eliminate all viable hemolytic streptococci. Shorter treatment may give a transiently negative throat culture, but, if the effective blood level is maintained less than 10 days, the cocci frequently reappear. Unless the streptococci are completely eliminated, rheumatic fever may occur.

For intensive therapy of an existing hemolytic streptococcic infection, the following regimens are recommended: (1) a single intramuscular injection of 600,000 to 900,000 units of benzathine penicillin G for children and 1,200,000 units for adults; (2) a buffered soluble salt of penicillin G, potassium penicillin O, or phenoxymethyl penicillin, 250,000 units by mouth two times daily for 10 days; or (3) procaine penicillin G with aluminum monostearate in oil, 300,000 units for children and 600,000 units for adults given intramuscularly every third day for three doses.

This form of prevention of rheumatic fever is so simple and direct that it is tempting to rely on it alone. Unfortunately, however, this cannot be done in a patient who has proved to be susceptible to rheumatic fever because of the well-known fact that, in close to 50% of attacks of rheumatic fever, the inciting hemolytic streptococcic throat infections are so mild that they may pass unnoticed. Hence, intensive therapy of throat infections is of value mainly as a "second line of defense" for the treatment of infections which may break through a carelessly followed regimen of continuous prophylaxis. Obviously, also, therapy is indicated in the treatment of any patient, with rheumatic disease or not, with a hemolytic streptococcic infection. Penicillin is used far too often for viral infections of the throat, in which it is ineffective. On the other hand, it is all too frequently given for too short a time in true hemolytic streptococcic infections. There can be no doubt that many first attacks of rheumatic fever could be prevented if adequate blood levels of penicillin were always maintained for a full 10-day period in the treatment of streptococcic pharyngitis.

Treatment of an Established Attack

In contrast to the important advances which have been made in the prevention of rheumatic fever, the current status of treatment of an attack which has already begun is confused and unsatisfactory. Indeed, there are few, if any, measures today which can be claimed with certainty as better than those available 50 years ago. In the remainder of this section, consideration will be given to various time-honored measures of treatment and to the following unsettled questions. Are the corticosteroids (glucocorticoids) and salicylates of value in the treatment of carditis, and, if so, are the former superior to the latter? Should both be used together? Does penicillin have a curative as well as a prophylactic effect?

Time-Honored Measures.—Among the time-honored measures of treatment are salicylates, rest, and various measures for the treatment of heart failure.

Salicylates: The great value of salicylates in the treatment of the polyarthritis and fever of rheumatic fever remains unchallenged. Indeed, there probably is no therapeutic response in all of medicine more striking than that of rheumatic polyarthritis to these drugs. On the other hand, in spite of opinion to the contrary by some European physicians, it was almost universally believed in the United States and Great Britain up to relatively recently that salicylates had little or no effect on rheumatic carditis. This belief was based on the frequent appearance and progression of severe carditis while the patient was taking full therapeutic doses of salicylates, and also on the fact that rheumatic nodules could appear during salicylate therapy. Since these lesions are made up of microscopic granulomas like those of the myocardial Aschoff bodies, it was assumed that the granulomatous type of inflammation in the myocardium also progressed in spite of salicylates. During the past five years this opinion has been questioned in the United States as discussed later. Meanwhile, however, there never has been doubt as to the dramatic value of these drugs in polyarthritis. For maximal suppression of inflammation, a blood salicylate level of 25 to 35 mg. per 100 cc. of serum should be maintained, but polyarthritis and fever usually respond to smaller amounts. A dosage of 5 to 8 Gm. given daily in multiple doses of 1 Gm. each will suffice for the adult in most instances. Children require relatively less. Their dose may be computed on the basis of 60 mg. per pound of body weight daily for one or two days, then 40 mg. per pound daily for a week or 10 days, followed by 30 mg. per pound daily for as long as symptoms persist.

Digitalis and Diuretics: In the presence of congestive heart failure, digitalis and diuretics are indicated as in any other type of heart disease. Greater caution must be taken in digitalization than in congestive failure due to other causes, however, because rheumatic myocarditis appears to make the heart more than normally susceptible to the development of toxic arrhythmias.

Rest: In the absence of any effective treatment for carditis, complete rest in bed has long been the measure principally relied on. Up to 15 or 20 years ago, very strict rules governing rest were insisted on in the United States, as they still are in a few centers, namely, that, before rheumatic patients are allowed to sit up, they must have a temperature, sleeping pulse rate, and laboratory indexes of inflammation which are completely normal without salicylates for at least 10 days, as well as absence of all manifestations of rheumatic fever. During recent years, however, more and more American investigators tend to adopt a far less strict policy regarding rest. This has come about for three principal reasons: 1. There has been a growing realization that complete bed rest is more apparent than real, especially in children, once the acute phase of disease is past. 2. Various studies have suggested that allowing the patient to sit up does not do harm and may even be helpful. 3. In any event, the psychological damage caused by insistence on bed rest over periods of months probably outweighs any questionable physical benefit. In order to obtain a sample of current opinion regarding rest, 22 leaders in the field of rheumatic fever in the United States and Canada recently were queried with the following results: 6 of them still insist on strict bed rest for any patient with rheumatic fever, whether or not carditis is evident; 2 have adopted a moderately liberalized interpretation of the rules, even when carditis is present; and 14 allow the patient to start sitting up for short periods and to be taken to the bathroom once or twice each day as soon as acute pain, congestive heart failure, pericarditis, and gross tachycardia have subsided.

Value of Corticosteroids and Salicylates in Carditis.—With the advent of cortisone (Cortisone, Cortogen, Cortone), hope was high that at last an agent was available which would suppress rheumatic inflammation not only in the joints but also in the heart. However, nine years after the introduction of corticosteroid therapy in rheumatic fever it still cannot be stated with absolute finality whether these agents are of value in carditis or, indeed, whether they may not actually be harmful. Despite reports of favorable results by many physicians, including the author, in preventing serious heart damage from rheumatic fever, only one controlled study which meets statistical standards has been made. This was the "Cooperative Clinical Trial of ACTH, Cortisone and Aspirin in the Treatment of Acute Rheumatic Fever in Children," carried out by the Rheumatic Fever Working Party of the Medical Research Council of Great Britain and the Subcommittee of Principal Investigators of the Council on Rheumatic Fever and Congenital Heart Disease of the American Heart Association. This careful study, based on 497 children with acute rheumatic fever treated at 12 centers in the United States, Great Britain, and Canada, failed to reveal any superiority of cortisone or corticotropin (ACTH, Acthar, Corticotropin) over aspirin, in terms either of the response of the acute disease or of heart damage after one year of follow-up.

In that study cortisone was given in total daily doses of 300 mg. for the first day, 200 mg. for the next four days, 100 mg. for the remainder of the first three weeks, 75 mg. for the fourth and fifth weeks, and 50 mg. for the sixth week. Because of the possibility that the corticosteroid dosage had been too low in the "Cooperative Clinical Trial," investigators from several of the participating centers joined with others in a similar clinical trial in which prednisone (Deltasone, Deltra, Meticorten, Paracort) was given in doses three to four times the equivalent of the previous therapeutic doses of cortisone for a period twice as long. Only children with clinically definite carditis in their first attacks of rheumatic fever in whom treatment could be started within the first three weeks of illness were included in the study. The actual daily dosage schedule of prednisone used was 60 mg. for the first three weeks, 50 mg. for the fourth week, 40 mg. for the fifth week, 30 mg. for the sixth week, and then gradual tapering over the next six weeks, so that the total amount given during the 12-week period was 3 Gm. The results in 24 children who received prednisone and 23 who received aspirin give no support to the view that corticosteroids in large doses over a three-month period have any greater effectiveness than do salicylates in reducing the incidence of residual cardiac damage at the end of one year of follow-up. Furthermore, the "rebounds" of transient signs of increased disease activity so frequently seen after shorter courses of corticosteroids in rheumatic fever were also apparent after the longer courses. No serious untoward effects were noted. However, in view of the lack of evidence of ultimate benefit and the acknowledged hazard of such large doses of corticosteroid, the group of investigators recently decided that continuation of the study was unjustifiable, and it has been stopped.

It was mentioned earlier that, after many decades of serious doubt in this country as to the value of salicylates in rheumatic carditis, there has recently been a trend toward a more optimistic attitude on the subject. Paradoxically, this has stemmed partly from the "Cooperative Clinical Trial of ACTH, Cortisone and Aspirin." When that study was designed, the group treated with aspirin was included to serve essentially as "untreated" controls from the standpoint of carditis. When close observation of the large number of patients studied showed that those treated with salicylates fared essentially the same as those receiving corticosteroids, the report concluded that "there was no evidence that any of the three agents resulted in uniform termination of the disease and on all treatments some patients developed fresh manifestations during treatment," and that "at the end of one year there was no significant difference between the three treatment groups in the status of heart." Nevertheless, in spite of this careful statement, it has frequently been assumed that the similarities in results in each treatment group meant that each treatment was helpful in lessening cardiac damage. Obviously, it might be concluded with equal reason that none of the treatments was effective. Since no completely untreated group was included, the study did not answer that question.

Assessment of the possible benefits that may be expected from corticosteroid or salicylate therapy in the various manifestations of rheumatic fever can perhaps be made clearer through consideration of the various phases of the disease process. These may be somewhat arbitrarily thought of under six headings: (1) the underlying mechanism of disease, (2) tissue injury, (3) the phase of acute exudative inflammation, (4) the phase of granulomatous inflammation, (5) the formation of scar tissue, and (6) the inactive phase of mature scarring. Considering these individually, there is no evidence that corticosteroids or salicylates affect either the underlying mechanism of disease or the stage of mature scarring. On the other hand, there is good evidence that both these agents strongly suppress the acute exudative inflammatory process. The evidence regarding suppression of tissue damage and of the granulomatous type of inflammation unfortunately is uncertain and conflicting. The subcutaneous rheumatic nodule can be cited as an example of a granulomatous lesion which can be seen and measured, yet reports as to the effect of corticosteroids on its evolution and disappearance are widely conflicting. A number of authors have reported the rapid disappearance of these nodules under the influence of cortisone and corticotropin, whereas others have noted no effect. In the "Cooperative Clinical Trial," new subcutaneous nodules appeared with approximately equal frequency during therapy with corticotropin, cortisone, and aspirin. In view of the conflicting conclusions regarding such easily observable lesions as subcutaneous nodules, it is not surprising that divergent results have been reported regarding the effects of corticosteroids on rheumatic carditis. Clearly, however, analysis reveals no unquestionable evidence of striking superiority of corticosteroids over salicylates, as judged by the ultimate development of organic valvular lesions. There remains the question of possible benefit which might be given by the proved capacity of corticosteroids to inhibit scar formation. That experimental effect in animals has been obtained, however, with far larger doses of corticosteroids than are used therapeutically. Again it must be concluded that the end-results of controlled studies do not suggest any greater prevention of valvular scarring by cortisone than by salicylates.

Summarizing this discussion of the possible effects of corticosteroids and salicylates on the various phases of rheumatic lesions, it would appear probable that only acute exudative inflammation is strikingly benefited. Thus, the value of these agents in the treatment of various manifestations of rheumatic fever probably depends largely on the severity of acute exudative inflammation. In rheumatic polyarthritis, in which this is the predominant feature and granulomatous lesions and scarring are minimal, corticosteroids and salicylates are extremely effective. In contrast, the acute exudative phase of inflammation probably is transient and of secondary importance in most instances of rheumatic valvulitis and myocarditis. Nevertheless, it is reasonable to hope that there may be some benefit in most patients with carditis if treatment can be started within the first few weeks of illness. In some patients with high fever and, especially, with severe pericarditis, agents capable of suppressing acute inflammation may be of great value.

Corticosteroids and Salicylates Used Simultaneously.—In view of the similar anti-inflammatory effects of corticosteroids and salicylates, many investigations have been carried out to test the possibility that the latter may act through stimulation of the pituitary-adrenal axis. From the standpoint of the treatment of rheumatic fever, the question is a practical one because, if salicylates act by stimulating an increased endogenous output of corticosteroids, there would be little reason to give the two together. On the other hand, if these agents act through different mechanisms, their simultaneous use in the same patient is reasonable. An abundant literature has already accumulated on the subject, with conflicting results and conclusions which it is unnecessary to review here. One may say in summary that the evidence does not support the view that the antirheumatic effect of salicylates is mediated through the adrenal cortex. It is, therefore, reasonable to use both agents together.

Intensive Penicillin Therapy.—Before discussing intensive penicillin therapy for rheumatic fever, it will be helpful to review very briefly the current views as to the possible mechanisms by which hemolytic streptococcic infections cause rheumatic fever. Four theories may be mentioned. According to one, the underlying mechanism is that of delayed hypersensitivity to streptococci or their products. According to the second, the disease results from autoantibodies to the patient's own tissue proteins which have been altered by streptococcic action. A third theory invokes the action, either direct or through the mechanism of delayed hypersensitivity, of a hypothetical specific toxin or enzyme common to "rheumatogenic" hemolytic streptococci. According to the fourth theory, the acute manifestations of rheumatic fever may have one of the aforementioned explanations, but the ultimate cardiac damage results from the persistence of living hemolytic streptococci, either as such or as "L" forms, which have invaded the heart muscle and valves.

The use of corticosteroids as outlined in the preceding sections is based on the hope of suppressing sterile inflammatory reactions resulting from such mechanisms as those underlying the first three theories. If, however, the fourth theory is correct, corticosteroids might be expected to be harmful because of their capacity to enhance the spread of infections. Therefore, intensive therapy with penicillin would be the logical attack.

Several studies carried out soon after the advent of penicillin indicated that, whereas this antibiotic was effective in preventing hemolytic streptococcic infections (and, hence, rheumatic fever), if taken daily throughout the year it did not benefit the acute manifestations of rheumatic fever if given after that disease had started. For some years the influence of these reports retarded any widespread use of penicillin in treating rheumatic fever until Massell's and Rammelkamp's demonstrations, previously referred to, that intensive use of a bactericidal agent like penicillin early in tonsillitis could prevent an ensuing rheumatic attack. After this there was gradual acceptance of the view that a similar intensive course of penicillin should be given early in rheumatic fever, with the aim of eliminating any hemolytic streptococci which the patient might still be harboring and which might tend to maintain rheumatic activity. During recent years this has become standard practice in the United States and in Great Britain. No experimental trial was made to test the value of such a regimen, however, until the studies reported in 1959 by Mortimer, Vaisman, Rammelkamp, and their collaborators. These investigators carried the concept a step further by giving a more intensive course of penicillin than that previously used. This procedure was designed to eliminate not only streptococci in the throat but also any which (according to theory number four) might have lodged in the cardiac tissues where, hypothetically, they might be more difficult to eradicate. These investigators have reported on a preliminary study of 85 patients in Santiago, Chile and have considered the results to be sufficiently promising to warrant further evaluation.

The regimen of penicillin used was the following: 500,000 units of sodium penicillin G intramuscularly every four hours for 10 days, followed by procaine penicillin G intramuscularly twice daily for 11 days, then 1,200,000 units of benzathine penicillin G intramuscularly on the 22nd and 43rd days, and thereafter at five-week intervals. These patients also received aspirin in doses of 75 mg. per kilogram of body weight daily for 14 days. No differences were noted in 42 patients treated in this way compared with 43 patients given the aspirin alone, so far as the effect on the acute manifestations of rheumatic fever was concerned. Furthermore, subcutaneous nodules, pericarditis, and heart failure were at least as frequent during therapy in the penicillin-treated patients as in those receiving only aspirin. On the other hand, one year later the former group showed a "statistically significant" lesser amount of organic heart disease than did the latter.

Obviously this study needs confirmation before its real significance can be known, for the regimen of penicillin employed may offer no advantages over those currently in general use. It has been pointed out that a basic part of the treatment of rheumatic fever in recent years has been prompt institution of penicillin in doses large enough to eradicate hemolytic streptococci from the throat. For this purpose, various treatment schedules have been used as outlined in the section on Penicillin Therapy. It has been assumed that, if the recommended doses are maintained for a minimum of 10 days, all viable hemolytic streptococci are eliminated in the great majority of patients because throat cultures subsequently are negative, and rheumatic attacks are prevented. Nevertheless, it may be that still more intensive therapy, approaching that used in the Santiago studies, is preferable in the case of the rheumatic attack which has already begun. Furthermore, if theory number four is correct and ultimate cardiac valvular damage in rheumatic fever does result from hemolytic streptococci harbored in the cardiac tissues, corticosteroid therapy could be expected to enhance their spread. Hence, on the grounds that are at present purely theoretical, it may be desirable to give penicillin fairly intensively throughout the period of corticosteroid administration.

Treatment of Other Manifestations of Rheumatic Fever.—In addition to fever, polyarthritis, and carditis, other less frequent manifestations of rheumatic fever include subcutaneous nodules, erythema marginatum, chorea, and pleurisy. The doubtful effect of corticosteroids and salicylates on subcutaneous nodules has already been discussed. It is generally agreed that these agents are without effect on erythema marginatum. Despite some reports of control of chorea minor (Sydenham's chorea) by moderate or massive doses of corticosteroids, most investigators believe that they are not effective and rely on rest and sedatives. Since inflammation of the acute exudative type often is a major component of rheumatic pleurisy, it is not surprising that this manifestation often appears to be benefited by corticosteroids and probably also by salicylates.

Patients with inactive rheumatic heart disease without heart failure, grossly abnormal cardiac rhythms, marked cardiac enlargement, or dynamically severe valvular lesions should not have their physical activities limited and should lead essentially normal lives. They should, however, be maintained on continuous prophylaxis against hemolytic streptococcic infections by one of the outlined regimens.

In the event of heart failure or important arrhythmias, appropriate measures should be instituted as is done for those manifestations in any other type of heart disease. Moreover, because of the possibility that such manifestations may indicate a fresh bout of rheumatic activity, evidence of the latter should be looked for, and, if found, intensive penicillin therapy should be given to eliminate any possible hemolytic streptococci which may be present.

Summary

Whereas the essential role of group A hemolytic streptococcic infections in causing rheumatic fever is now definitely established, the exact mechanism by which these infections cause the disease is not yet known. Advances of the utmost importance have been made in the prevention of rheumatic fever, including continuous prophylaxis for many years, designed to prevent the inciting hemolytic streptococcic infections, and intensive, early penicillin therapy of any hemolytic streptococcic infection which may occur.

In contrast to prevention, few advances of definitely proved value have been made in the treatment of the rheumatic attack which has already begun. Certain conclusions can be drawn, however, as follows.

1. The early hope that corticosteroid therapy could control rheumatic carditis and prevent lasting cardiac damage has not been borne out, and experience indicates that large doses given for long periods are hazardous and probably do more harm than good. It can be stated with considerable assurance that corticosteroids do not control the underlying, unknown mechanism of the disease and do not prevent the progression of permanent valvular damage. They have great capacity to suppress rheumatic polyarthritis and fever, but the same effects can be achieved with equal rapidity and greater safety by means of salicylates. It is possible that corticosteroids may be of value early in carditis through suppression of the acute phase of inflammation, although it has not been proved that they are more effective even for this than are full doses of salicylates.

2. Since group A hemolytic streptococci have been proved to incite rheumatic fever, it appears logical and important to eliminate early in the course of rheumatic fever any hemolytic streptococci that may be present, even though throat cultures may be negative. It is equally important to prevent any new infections by these micro-organisms.

On the basis of these principles the following regimens are suggested for the therapy of rheumatic fever.

1. Prompt and intensive therapy with penicillin should be instituted to eliminate any hemolytic streptococci which the patient may be carrying. For this purpose, any of the regimens outlined in the section on Penicillin Therapy probably is sufficient. However, in view of the theoretical possibility that hemolytic streptococci in the heart may be a factor which leads to ultimate valvular damage, and on the hypothetical assumption that they may be more difficult to eradicate there than in the pharynx, it may be preferable to administer larger doses than those recommended for the treatment of streptococcic infections of the throat. It must be emphasized, however, that there are as yet no data to indicate that, at the outset of the rheumatic attack, larger doses of penicillin are superior to those which have been recommended for the intensive treatment of a hemolytic streptococcic throat infection. It may be advantageous also to continue throughout the period of corticosteroid administration somewhat larger doses than are usually given for continuous prophylaxis, but current information does not warrant including this as one of the essential recommendations. For the latter purpose, 1,200,000 units of benzathine penicillin G could be given intramuscularly every two weeks rather than every four weeks as long as corticosteroids are being administered.

2. If carditis is not evident, it is suggested that salicylates be used without corticosteroids, in the doses which have been outlined.

3. If carditis is present and treatment can be started within the first 3 weeks of onset, most investigators believe corticosteroids should be given. For this purpose, prednisone (or other corticosteroids in equivalent amounts) may be given in doses of 10 mg. four times daily by mouth for 10 days. Thereafter the total daily dose may be reduced at the rate of 2.5 mg. daily until discontinued. Again, on rather empirical grounds, it is suggested that aspirin be given with the corticosteroid at the rate of 900 mg. five to six times daily for adults and on the basis of body weight for children, as described. The salicylate should be continued after corticosteroid has been stopped, as long as symptoms, fever and erythrocyte sedimentation and C-reactive protein tests (or other tests for acute phase reactants) suggest continuing disease activity. The evidence for the value of corticosteroids even early in carditis is questionable. If they cannot be begun within the first three weeks of onset of the carditis or of a new exacerbation, this form of therapy probably is not warranted.

4. Although complete bed rest is necessary during the period of acute symptoms, most American investigators believe that, once this stage is past the patient may be allowed to sit up each day whether or not carditis is present. If carditis is not present, gradually increased walking can then be allowed. In attacks associated with carditis, however, walking probably should not be permitted until convalescence is well advanced.

5. Continuous prophylaxis begun during the acute illness should then be maintained; one of the regimens outlined should be followed, with the intention of keeping it up indefinitely.

Patients with inactive rheumatic heart disease and without cardiac insufficiency or grossly abnormal rhythms should not have their physical activities limited but should be on a regimen of continuous prophylaxis. Heart failure and arrhythmias call for the same measures as in other types of heart disease; in addition, it is recommended that, at their appearance, the patient be given a course of intensive penicillin therapy on the chance that they indicate a breakthrough of hemolytic streptococci and a new attack of low-grade carditis.

It must be emphasized that, whereas the regimens for prevention of rheumatic fever can be recommended with assurance, most of those for treatment of the rheumatic attack are unproved and are presented as reasonable measures in the light of what is known and what is not known about rheumatic fever today.

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Report to the Council

The Council has authorized publication of the following paper, which was presented as part of a symposium-panel discussion held in Washington, D. C., Sept. 25, 1958, on the Use and Abuse of Adrenal Steroids. This is the second paper in the series, the first of which appeared in THE JOURNAL *on June 20, 1959, page 951.* H. D. KAUTZ, M.D., *Secretary.*

STEROID THERAPY IN RHEUMATOID DISEASES

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Ten years have elapsed since cortisone (Cortisone, Cortogen, Cortone) acetate was first given to a patient with rheumatoid arthritis. This occurred on Sept. 21, 1948, at the Mayo Clinic under the direction of the team composed of Drs. Hench, Kendall, Slocumb, and Polley.[1] Spearheaded by the immediate spectacular changes in the symptomatology of rheumatoid arthritis, there resulted a great increase in interest in the field of rheumatic diseases, with expanded research and improved care for the arthritic patients. Also, as a result, there has been a search for better understanding of the underlying immunological and pathological states in these diseases.

This discussion concerns rheumatoid diseases which include gout, acute rheumatic fever, rheumatoid spondylitis, collagen or connective tissue diseases, and rheumatoid arthritis.

Gout and Gouty Arthritis

Adrenal cortical steroids have been used orally in the treatment of acute attacks of gouty arthritis since 1949, with varying grades of effectiveness. In some patients the results were excellent, but in other patients only a mild degree of improvement was obtained. Because of lack of uniformity of relief of acute gouty arthritis, the adrenal steroids have not been used routinely. However, recently in our experience, a combination of 0.5 mg. of colchicine with 8 mg. of triamcinolone (Aristocort, Kenacort) taken every two hours for four doses has been consistently effective. This is repeated the following day only if necessary. Complete relief of pain and swelling has occurred in all acute attacks. No untoward reactions or side-effects to either drug have been observed.

Although corticotropin (ACTH, Acthar, Corticotropin) is not an adrenal steroid, it stimulates their production and should be discussed. It has been used with uniformly satisfactory results in the treatment of the acute attack of gouty arthritis. A dose of 40 to 60 U. S. P. units intramuscularly two or three times a day for several days, or a single injection of 100 to 120 U. S. P. units of purified corticotropin (ACTH, Purified; Depo-ACTH; Purified Corticotropin) gel, or the intravenous use of 20 to 40 units has been effective. This method is used in those who are unable to take medicaments by mouth such as the patient after operation as well as those who seek treatment when oral therapy has been ineffective, as in a particularly difficult flare-up involving multiple joints. The drug is given intravenously each day over a period of six to eight hours, as the half-life of corticotropin is 1 to 17 minutes. This procedure should be followed by 0.5 mg. of colchicine twice daily for 10 to 14 days to prevent rebound attacks.

Acute Rheumatic Fever

The influence of the adrenal cortical steroids in rheumatic fever must be evaluated from two standpoints. One is the immediate effect on the signs and symptoms of the disease during the acute phase and the other is the influence on cardiac involvement when measured two or more years after the acute attack.

Many physicians who treat acute rheumatic fever prescribe large amounts to the patient as soon as the diagnosis is suspected or confirmed. The earlier it is given the greater the possibility it will be effective, certainly not later than three weeks after onset of the disease. There is usually prompt suppression of the clinical manifestations, i. e., arthritis, fever, and tachycardia. The drug should be given in generous amounts as long as this suppression is necessary. The dosage should be varied, depending on the activity of the rheumatic fever, and stopped altogether when the clinical manifestations have subsided.

The greater benefit has been observed in the patient's cardiac status several years after the acute episode. If such an attack is treated early and with adequate doses, the incidence of rheumatic heart disease is lessened. This is very encouraging, as it appears to be a milestone in the prevention of car-

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diac complications such as heart failure in later life. Here, again, it is necessary to emphasize the use of adrenal steroids early in the attack of acute rheumatic fever in order to derive the greatest benefits.

Rheumatoid Spondylitis

There are some patients who require the use of adrenal steroids in rheumatoid spondylitis from time to time. The general application is similar to the use of adrenal steroids in rheumatoid arthritis and will be discussed under that heading.

Osteoarthritis

Although osteoarthritis is not a rheumatoid disease, adrenal steroids, when used intra-articularly, may be effective in relieving pain and swelling. An injection, into the joint space or into the periarticular structures, of hydrocortisone (Cortef, Cortril, Hydrocortisone, Hydrocortone) acetate, prednisolone butylacetate (Hydeltra-T. B. A.) or methylprednisolone (Medrol) often produces prompt as well as lasting improvement. Any peripheral joint can be injected easily, including the proximal interphalangeal joints. Although the hip joint responds least well of all the joints, a sufficient number are benefited to warrant a trial. The patient who has one or two painful joints due to osteoarthritis should receive two or three intra-articular steroid injections. The time interval is determined by the relief of symptoms. In Hollander's[2] series of over 74,000 injections, complications were rare. The oral administration of adrenal steroids in osteoarthritis is of little or no value.

Collagen or Connective Tissue Diseases

Inasmuch as this group of disorders may have rheumatoid changes as part of the complete syndrome, it should be included in this report. In general, it is assumed that the administration of adrenal steroids is suppressive. Some physicians believe that life may be prolonged by steroids when given to patients affected with a mild or moderately severe collagen disorder. There is general agreement that, during acute episodes, their use is definitely indicated and may be lifesaving. During this phase large doses should be given in order to control the clinical state of the patient. Also, if one steroid does not appear to be effective, others should be tried, as there may be a difference in response in certain patients. After the acute episode the dosage should be reduced to a minimum or eliminated altogether, if possible. Therefore, it is advisable to use adrenal steroids only at such times in the treatment of collagen or connective tissue diseases as the patient requires them for acute symptoms not controlled with other medication.

Rheumatoid Arthritis

The suppression of the signs and symptoms of rheumatoid arthritis after the administration of adrenal cortical steroids startled the medical profession. Incentive for research in arthritis, as well as in many other fields, followed. Physicians had renewed interest in arthritis, which led to improved medical care for the patient. As the result of 10 years' experience, the adrenal cortical steroids are not used routinely in the treatment of rheumatoid arthritis but only during certain phases of the disease, as listed later. Despite various schedules of dosage, the effect of these drugs is temporary. Within 48 hours after cessation of therapy, most patients revert to the previous arthritic state. There is no dose of these steroids low enough to produce clinical improvement without the development of side-effects in the patient. The usual complication is that of clinical hypercortisonism as evidenced by adrenal cortical hyperfunction (Cushing's syndrome), with one or more of the changes such as moon face, buffalo hump, hirsutism, striae, glycosuria, hypertension, and osteoporosis. These may occur in various degrees.

Most physicians are convinced that a basic program of management is the proper plan of therapy for the patient with rheumatoid arthritis. This includes a period of complete bed rest and physical therapy and analgesic medication administered with sincere, interested, medical attention. There is an increasing return to gold therapy as part of this program.[3] Adrenal steroids are not given routinely to the patient with mild or moderate joint involvement, as the course of the disease is frequently controlled with "conservative" treatment. Inasmuch as the adrenal steroids are only suppressive, the patients under their influence have a false sense of security. At that time they are apt to be too active physically, thus mechanically aggravating the underlying arthritis without warning to the patient. In addition, the ulcerogenic tendency (whether it refers to a new or reactivated ulcer) complicated by hemorrhage or perforation, along with masking of infections, purpuric manifestations, and production of adrenal inactivity or atrophy may be serious complications when adrenal steroids are given over a long period of time. However, there are several phases during the course of rheumatoid arthritis when adrenal cortical steroids should be used to the permanent benefit of the patient. They should be given a thorough trial under the following conditions:

1. The patient with severe rheumatoid arthritis deserves a trial with adrenal steroids. Often great relief can be obtained with small amounts. The attending physician must visit the patient regularly to adjust the dose of the steroids, depending on the effectiveness of therapy. Often a patient who is in

great pain and discomfort may experience marked prolonged improvement with minimal amounts. Even with small doses of steroids, however, it is expected that side-effects will appear sooner or later. In this group of patients, most of them will do very well as soon as a minimum dosage is established in relation to the side-effects the patient is willing to endure in order to obtain relief of symptoms.

2. Patients who, during the course of the disease, have severe constitutional signs of tachycardia, anemia, fever, and weight loss will need steroids in large amounts. They may save the lives of some patients. Often these exacerbations are of short term, perhaps several months, after which the steroids may be discontinued entirely. A higher percentage of those with juvenile rheumatoid arthritis will experience this type of exacerbation than those with the adult type. It is in these patients, also, that it may be necessary to shift from one steroid to another in order to obtain the maximum effect. The administration of steroids to these patients is mandatory.

3. During the course of gold therapy some patients develop dermatitis, which does not improve on cessation of the gold salt medication nor respond to other measures. Such patients will often derive great benefit when given an adrenal steroid to control the itching and irritation due to the dermatitis.

4. One of the greatest uses of adrenal steroids is in the group in which a program of rehabilitation has been planned. This is especially helpful when measures are used to attempt to extend completely a partially flexed joint, such as the knee, during the first time a cast is applied. Usually much time is saved, as greater range of motion is possible when the patient is receiving steroid medication. This should be administered intra-articularly as well as orally. The adrenal steroid is started one week before, and discontinued within two weeks after, application of the cast. Another phase of rehabilitation which is made easier by use of adrenal steroids is during the time that the patient is trying to learn exercises or to use apparatus such as the wheel or wands. Also, exercises for non-weight-bearing muscle are much easier to teach when the patient is receiving steroid therapy.

5. The intra-articular use of steroids is important; in many cases, the action appears to be more than suppressive, as excellent responses may persist for long periods. Range of motion is increased, swelling recedes, and pain is lessened. Steroids should be administered intra-articularly to the patient when one or two joints are more troublesome than the others. It is necessary to inject the drug into the joint space to obtain the best results. However, infiltration of the periarticular structures of the phalangeal joints or the elbow joint may also produce a favorable response. Reactions are unusual with this route of administration, provided strict surgical asepsis is followed. The most satisfactory improvement after injection of steroids occurs in the joints of fingers, elbows, and knees. The frequency of injections is governed by return of symptoms; they may be given weekly or at longer intervals. If there is no improvement after three weekly injections, this type of treatment should not be continued. Again, it must be emphasized that every effort must be made to inject the adrenal steroid intra-articularly in order to obtain the most relief.

Adrenal steroid therapy should not be used routinely during the initial treatment of rheumatoid arthritis, especially if the disease is mild or moderate in severity. Conservative measures should be used first. Steroid therapy should not be given along with gold salt therapy, as it tends to nullify the beneficial effects of the gold.

The physician assumes a great responsibility when he initiates the use of adrenal cortical steroids in a patient with rheumatoid arthritis. Generally, with the exceptions stated previously, the effect of these steroids is temporary, having little or no permanent benefit on disease structures in or around the affected joints. However, the patient does feel so much better for a varying period of time, extending for months, that continued use is most pleasant for the patient. However, there comes a time when the symptoms are not controlled, despite increased dosage, and, at that point, the patient becomes one of the most difficult problems in rheumatology. After weeks of attempts to discontinue administration of steroids, some patients are comfortable with gradual prolonged reduced dosage of the steroid to the point where no more is necessary and other analgesic medication is substituted. But many patients will never stop using steroids, and life becomes a more unpleasant problem than ever. It is in these patients that the most serious complications of adrenal cortical steroid therapy are most apt to occur. Therefore, in the patient with mild or moderate rheumatoid arthritis, it is highly desirable to outline a conservative program of management, including gold salt therapy, before any steroids are given.

Before concluding this discussion it is appropriate to describe some of the common reactions to prolonged administration of adrenal cortical steroids or corticotropin.

1. Cushing's syndrome of clinical hypercortisonism may develop, consisting of moon face, buffalo hump, hirsutism, striae, and edema. These signs usually disappear after discontinuance of the drug. However, glycosuria and hypertension, also part of this syndrome, may be permanent.

2. Negative nitrogen, calcium, or phosphorus balance may occur, with subsequent osteoporosis which may lead to bony fractures. The concomitant use of anabolic hormones, especially in the postmenopausal woman, is desirable if prolonged administration of the steroids is necessary.

3. Gastrointestinal complications may develop into a serious disability. Peptic ulcers may develop or become reactivated, with complications such as bleeding and perforation. It is necessary to keep the contents of the stomach alkaline or at least neutral by the administration of antacid with each dose of steroid to prevent peptic ulcer formation.

4. Masking of infections is not uncommon. Fever or other complications such as perforation may not be detected. There is an interference with normal immune processes of the body, and unrecognized septic processes may develop rapidly or even result in death. The early use of antibiotics is necessary. Acute appendicitis, perforation of a peptic ulcer, or a diverticulum can occur—only to be recognized too late to save the life of the patient. Apparently the adrenal cortical steroids interfere with the normal mechanism of immunity, causing the unrecognized septic processes to occur.

5. Flushing of the face and purpuric spots in the skin are more common with the newer steroids. In some instances, these areas may be 3 to 4 cm. in diameter. The outer layer of the skin may rub off easily.

6. The production of adrenal inactivity or atrophy endangers the patient during periods of extra stress which may occur during fatigue, infections, or surgical procedures. The patient needs protection with the adrenal cortical steroid during stress for months after original therapy has been discontinued. In some patients it is necessary to use the adrenal cortical steroids parenterally.

7. There is the possibility of changing host-tissue responses so that the patient develops vascular angiitis, polyarteritis, or other collagen diseases. There is no positive proof at this time, but the evidence is strongly suggestive.

8. Patients with rheumatoid arthritis must be warned that excessive activity is to be avoided; otherwise the arthritis may worsen during the period of steroid therapy, as warnings of pain and swelling may be concealed for a time.

Summary

Ten years' experience is now available with the use of the adrenal steroids in the treatment of the rheumatoid diseases. During this period a variety of new adrenal steroid compounds have been developed, with the hope of making available for general use substances devoid of the potential for producing certain complications. To date, it has not been possible to accomplish this end. It has therefore become important to recognize the risks incurred with long-term use of the adrenal steroids as weighed against theoretical advantages. It would appear at the present time that these risks, in general, outweigh any advantages. Therefore, in the individual case, careful consideration is essential before beginning administration of adrenal steroids. The clinical situations in the field of rheumatic and collagen vascular diseases in which the long-term use of the adrenal steroids appears justified are actually few if indications are carefully appraised prior to their use.

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NEW AND NONOFFICIAL DRUGS

The following descriptions of drugs are based upon available evidence and do not in any case imply endorsement by the Council.

H. D. Kautz, M.D., *Secretary.*

Tuberculosis Vaccine (Tuberculosis Vaccine).—BCG vaccine.—Bacillus Calmette-Guérin vaccine.—A freeze-dried preparation of the culture of an attenuated strain of bovine tubercle bacillus, Mycobacterium tuberculosis, originally isolated by Calmette and Guérin. It is standardized in accordance with requirements of the National Institutes of Health.

Actions and Uses.—Tuberculosis vaccine, first licensed for general distribution in 1950, is proposed for use as an immunizing agent in the prevention of tuberculosis. Its use for this purpose is based on the ability of the vaccine to induce a positive tuberculin skin test reaction in a high percentage of individuals who are initially nonreactive to such a test. Conversion of negative tuberculin-tested subjects to positive reactors after vaccination is generally regarded as presumptive evidence of the development of immunity similar to that which follows a naturally resisted or healed primary sensitizing infection. Accordingly, tuberculosis vaccine is intended for, and should be used only in, individuals initially nonreactive to tuberculin.

Evaluation of the effectiveness of tuberculosis vaccine is hampered by the fact that skin reactivity to tuberculin does not measure the degree of immunity or amount of resistance to the disease. Moreover, there is no suitable quantitative method, such as a humoral test for antibodies, by which this can be estimated. Studies comparing the incidence of tuberculosis between vaccinated and nonvaccinated population groups indicate that the effectiveness of the vaccine in the prevention of the disease ranges from 50 to 80%, depending on the degree of exposure to active infection and other factors which influence susceptibility to the disease. Some authorities attribute variations in the results of vaccination to a lack of uniformity of the vaccine; others believe that a low degree of native resistance is associated with a correspondingly low response to vaccination. The duration of vaccine-converted tuberculin reaction varies according to age of the person. In newborn infants the reaction has remained positive for six to seven years (80%), whereas in medical students and nurses 70% were positive after two to three years. Most authorities agree that revaccination is advisable whenever tuberculin retesting shows that reversion to a negative reaction has occurred.

Indications for the use of tuberculosis vaccine are complicated by a lack of agreement concerning its importance in the over-all epidemiologic control of the disease. Some authorities believe that all tuberculin nonreactors, young and old, should be vaccinated and revaccinated as necessary, to induce and maintain a tuberculin-positive state. Other authorities take the position that the vaccine does not produce a high degree of protection and its employment is of minor significance as compared to control programs designed to improve the general level of health, including case-finding and isolation, and early treatment of open cases of the disease. Still others oppose widespread use of the vaccine because the artificial conversion to tuberculin-positive of large numbers of unexposed nonreactors vitiates the use of the tuberculin skin test as a diagnostic screening tool for early detection and treatment of infection; however, the claim is made that a differentiation between virulent infection or disease and vaccination can be established in a high percentage of cases. There is a large body of expert opinion which favors vaccination only for (1) children and adults considered to have inferior resistance and who reside in areas where the incidence of tuberculosis is high, (2) professional and other individuals whose work (as in hospitals) involves a high risk of exposure, (3) members of households unavoidably exposed to infectious cases in the home, and (4) inmates and personnel of institutions in which tuberculosis is found to be prevalent. Thus, among individual nonreactors to tuberculin, physicians have a choice either of using the vaccine to reduce the risk of clinical disease or of not using the vaccine and having the tuberculin skin test for early diagnosis and as a guide to the need for further study and treatment.

Tuberculosis vaccine as presently standardized and distributed in the United States is considered to be relatively free from untoward effects. The freeze-dried preparation is regarded as relatively stable for a period of six months, if kept refrigerated at 4 to 6 C, protected at all times against light, and used within two hours after resuspension. Local infection at the site of inoculation and/or regional lymphadenopathy may occur occasionally. Such reactions are considered more apt to follow the intradermal injection technique than the multiple puncture or scarification methods of inoculation. The vaccine is contraindicated in persons who have not been tested and found tuberculin-negative within the preceding two weeks, who are acutely ill or suspected of having a respiratory infection, who have received antibiotic medication within the past month, or who have an active skin disease. Tuberculin testing also is contraindicated in the presence of any acute illness, scabies, allergic dermatitis, or psoriasis; it is also contraindicated if a smallpox vaccination has been given within the previous month. The latter is significant because of the danger of cross infection between the sites of two similar types of vaccination.

Dosage.—Tuberculosis vaccine is usually administered by multiple puncture or by intradermal injection. Because the vaccine is composed of viable organisms and contains no preservative, it must be handled in a sterile manner. Ethyl alcohol 70% (undenatured) and/or acetone is used for cleansing of the site of the inoculation and the hands of the operator. Needles, syringes, or other equipment should be sterilized between each use by autoclaving, dry heat, or boiling water.

The dosage for adults and children is the same and is measured in drops of the resuspended vaccine (50 mg. per cubic centimeter) for the multiple puncture method of inoculation. The vaccine is placed directly on the cleansed skin at the inoculation site, usually over the left deltoid region. The required number of drops for each inoculation depends on the gauge of the needle or other opening from which the vaccine is deposited on the skin: 22 gauge, 4 drops; 17 gauge, 2 drops; syringe without needle, 1 drop. When single-dose capillary tubes are used, the resuspended contents of one tube are used for each inoculation. The multiple puncture method can be carried out by means of a specially constructed disk, which makes all punctures simultaneously, or with a needle used to make three rows of 10 separate punctures, 2 mm. apart. After inoculation by multiple puncture the site is allowed to dry without dressing and should not be washed for 24 hours. For intradermal injection, 0.1 cc. (equivalent to 0.2 mg.) of the resuspended and further diluted vaccine is injected as superficially as possible with a tuberculin syringe and a 26-gauge needle so as to produce a wheal of 8 to 10 mm.

In screening candidates for vaccination, the tuberculin test is usually read after an interval of 48 to 72 hours. A tuberculin test read after 48 hours should be performed eight weeks after vaccination and at six months to yearly intervals thereafter. Vaccinated persons found to be nonreactive should be revaccinated within two weeks of a negative tuberculin test. A single dose of 0.1 mg. (0.1 cc. of a 1:1,000 dilution) of old tuberculin is used for the first eight-weeks test after vaccination. Subsequent retesting should be done with two test doses as follows: first, 0.1 mg. (0.1 cc. of a 1:1,000 dilution) or 0.02 mg. (0.1 cc. of a 1:5,000 dilution), and if negative, then 1 mg. (0.1 cc. of a 1:100 dilution).

The tuberculin-positive skin reaction usually induced by vaccination is less pronounced than that found in the presence of active disease. Induration is less marked, and redness is less intense or absent. Accordingly, care must be taken in reading the test to palpate the actual site of injection. The proper site for testing is the upper third of the volar aspect of the forearm, preferably in a small hollow, and never over a muscle belly, tendon, or vein, so as not to obscure the detection of a positive induration. A reaction is considered positive when the area of induration equals or exceeds 6 mm. in any diameter.

Preparations: powder (freeze-dried) 50 mg. for resuspension to 1 cc. (14 doses by multiple puncture disk and 250 doses by the intradermal route) and capillary (single dose) units.

The Institution for Tuberculosis Research of the University of Illinois, the Research Foundation of Chicago, the City of Chicago Municipal Tuberculosis Sanitarium, and the Cook County Hospital cooperated by furnishing scientific data to aid in the evaluation of tuberculosis vaccine.

COUNCIL ON FOODS AND NUTRITION

Report to the Council

DIET IN THE MANAGEMENT OF PEPTIC ULCER

Harrison J. Shull, M. D., Nashville, Tenn.

The Council has authorized publication of the following report. This article is part of a nutrition education program which is assisted by the Nutrition Foundation, Inc.

PHILIP L. WHITE, Sc.D., *Secretary.*

The use of diet as an important part of the therapeutic regimen for the patient with peptic ulcer is a deep-rooted practice. In the first century A. D. Celsus prescribed a smooth diet, free of acrid foods at a time when little was known about disease of the stomach, and, as early as the seventh century, A. D., practitioners believed in the healing properties of milk when taken by patients whose digestive symptoms as then described suggested the likely possibility of peptic ulcer.[1]

In 1820, Christopher R. Pemberton[2] observed that certain patients had increased pain in their abdomen when their stomachs were empty. He did not recognize the existence of peptic ulcer. Nevertheless, he believed that altered stomach secretion irritated the nerves of the stomach, thus causing pain, and that food and certain alkaline drugs were capable of counteracting this altered secretion and thereby relieved the pain. Thus, it seems that Pemberton was among the first to propose the principles of the medical treatment of peptic ulcer that are adhered to at the present time.

During the succeeding half century peptic ulcer became established as a pathological and clinical entity. Jean Cruveilhier,[3] in 1856, is generally credited with being the first to emphasize the value of the so-called milk diet. The liberal and frequent feedings for peptic ulcer, that were advocated by the early 19th century physicians, were later replaced by a radically different plan of management. It was based upon the belief that when ulcer is present the stomach needs complete rest and that complete rest is attained only when the stomach is empty.

This notion, which stemmed first from Von Ziemssen and later was championed by Leube and Ewald, was introduced into the United States by Einhorn. In 1904 Herman Lenhartz disagreed. He

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From the Department of Medicine, Vanderbilt University School of Medicine.

advocated abandoning the initial starvation period of Leube and associates and urged the early feeding of patients with peptic ulcer.[4] However, these principles were not generally accepted by contemporaries of Lenhartz. It remained for Bertram Sippy,[5] in 1915, to establish once and for all the importance of continuous control of gastric activity through the use of dietary and medicinal methods.

Many changes in the details of management of peptic ulcer patients have occurred since Sippy's day. Although accepted practice throughout the world subscribes to dietary restriction of varying degrees, accumulating experience has challenged the validity of some of these beliefs. Todd[6] has asked some searching questions concerning the usefulness of diets as they are ordinarily prescribed. He states: "There is no proof that the avoidance of certain foods thought to be irritating, unless they cause immediate distress, is beneficial. There is no proven virtue in special diets over and above their influence in diminishing the acidity of the stomach." Gill[7] reported a series of studies of 20 consecutive patients with chronic gastric ulcer who were treated only with daily injections of 1 cc. of distilled water. No restrictions of activity or eating habits were imposed, and no medicines were given. Healing was observed to take place in four to eight weeks. Gill concluded: "Ulcers are not healed by diet alone, nor by injections, nor by medications but because the man with the ulcer comes under the care of a physician who is able to transmit some of his own confidence to the patient."

Lawrence[8] studied 140 patients with duodenal, gastric, and anastomotic ulcers. He concluded that rigid dietary treatment as it is presently practiced does not hasten peptic ulcer healing. Doll, Friedlander, and Pygott[9] carefully observed 121 patients with gastric or duodenal ulcers on a controlled dietary experiment. They stated: "Dieting with bland foods does not increase the rate of healing of peptic ulcer." Investigators in the United States have demonstrated in large series of patients that satisfactory healing in peptic ulcer disease can be obtained on a regimen which includes considerable liberalization of the diet as conventionally prescribed.[10] Rae and Allison[11] were able to study a group of Royal Navy personnel under particularly favorable circumstances over a six-year period. They pointed out that the natural history of peptic ulcer disease is an important factor in determining the rate of recurrence of ulcer activity, even under virtually ideal conditions for management.

Physiological Basis for Treatment of Ulcer by Diet

The fundamental cause of peptic ulcer is not clear. In the ulcer patient, it appears that the ability of the mucosa of the stomach or duodenum to withstand the digestive action of the acid gastric juice diminishes. In the patient with duodenal ulcer, excess production of acid and pepsin seems to be the paramount factor, whereas in the gastric ulcer patient, though the presence of hydrochloric acid and pepsin is essential, decreased tissue resistance may be more important. Since hydrochloric acid in the gastric juice is generally acknowledged to be an essential factor in the genesis, perpetuation, and recurrence of peptic ulcer, accepted therapeutic regimens, both surgical and medical, now have as one of their chief aims the reduction of hydrochloric acid. It is further believed that the pain experienced by the patient with an active ulcer of the duodenum or the stomach is related to the presence of unneutralized hydrochloric acid together with hypermotility of the duodenal or gastric walls. Thus, relief of this pain serves as a useful practical measurement of the effectiveness of a medical regimen that is aimed at reduction of gastric acid.

One of the accepted medical measures for effectively reducing gastric acid is the prescription of a dietary regimen. Conventionally, this diet is composed of those foods that, in so far as is possible, either inhibit the gastric secretory function or neutralize the acid gastric juice. Milk, cream, and products that include these substances have become prominent in most dietary prescriptions. These foods have a high acid-buffering capacity, and the fat in cream inhibits gastric secretion through the enterogastrone mechanism. It is also common practice (though its validity is being questioned) to exclude from the diet those foods that theoretically may be chemically, mechanically, or thermally irritating to the mucosa of the stomach or duodenum. This would include such foods as condiments, raw fruits or vegetables with seeds or high-residue content, and substances that are either very hot or very cold.

Some caution is also urged, especially in the early phases of treatment of an active ulcer, in regard to type and quantity of meat and meat extractives prescribed, since these are believed to enhance gastric secretion by their effect on the antral mucosa through the gastrin mechanism. Restraint in quantity of food taken at one time is suggested, since overdistention of the stomach is thought to further stimulate acid secretion and gastroduodenal hypermotility. Frequent feedings taken at regular intervals are employed so as to minimize acid during as many of the waking hours as possible.

The diet in peptic ulcer must be nutritionally adequate. This tenet is axiomatic. Whatever diet is chosen for the management of peptic ulcer, that diet should be, first of all, adequate in its nutritional qualities. If for any reason a diet deficient in the essential substances such as vitamins and minerals must be utilized for a time, the patient should be given supplementary substances to make up for the deficit. The importance of adequate nutritional elements for the reparative processes in acute or chronic ulcer without complications is very real. In seriously ill patients and especially in those with complications requiring either preparations for surgery or postoperative care, this need becomes urgent. An ulcer diet, as generally accepted and prescribed in the United States for the past two decades, provides a nutritionally adequate daily intake of simple, easily digested foods such as dairy products, selected tender meats, vegetables, and fruits, to be eaten in reduced quantities at frequent and regular intervals throughout the waking hours.

Psychological Factors Favoring Ingestion and Digestion

Present-day physicians are increasingly urging that the range of prescribed foods be broadened so as to provide for attractiveness, easy availability, and more normal living for the ulcer patient. The circumstances under which the food is eaten should be conducive to physical and emotional relaxation. It is probable that psychological factors favoring the ingestion and digestion of food approach, in importance, the actual choice of the foods. That this may be true is strongly indicated by observations of Wolf and Wolff.[12] The fistulous stomach of their subject retained part of a normal breakfast five to six hours when eaten under favorable and pleasant conditions. When the same breakfast was eaten under circumstances productive of anxiety and tension, the stomach was empty after four or five hours, and it exhibited engorgement of the blood vessels of the mucosa, increased acid production, and active motility.

Selection of Diet

A few generalizations will serve to illustrate the use of diets in the management of peptic ulcers, with varying degrees of activity.

Acute Ulcer.—For the active, acute duodenal or gastric ulcer, hourly feedings during the waking hours may be employed. Feedings consisting of three to four ounces of a mixture of two-thirds milk and one-third cream usually allay pain promptly. Such a mixture is deficient in proteins, vitamin C, niacin, thiamine, and iron. It should, therefore, not be used long without suitable supplementation of those nutrients in which it is deficient. In practice, as soon as pain is relieved, usually in several days, additional foods are added which make the diet no longer deficient in any nutrient. It may be desirable, especially if night pain has been a problem, to awaken the patient once or twice during the night for additional feedings.

Very infrequently, pain may not entirely disappear even after three or four days on this feeding program. Under such circumstances, continuous intragastric drip of the same milk and cream mixture for a few days may be more effective. The substitution of small feedings of soft foods for some of the milk and cream feedings may be used to help break the monotony. When pain disappears, the intervals between feedings are gradually lengthened, and an increase in the volume of food and a liberalization in the choice of foods are allowed. After a week or two, the patient will be established on a schedule of six feedings daily. Most of the foods commonly eaten in the American diet are gradually added to feedings of the basic milk and cream mixture. Obviously, the intelligent patient will avoid those foods that he knows from experience cause him to have indigestion, heartburn, pain, or other digestive symptoms. Coffee and alcohol are prohibited. Thorough mastication of all foods is in order.

Should perforation or obstruction occur, food and water by mouth, as well as orally given medicaments, should be withheld until other appropriate measures have been effected, such as surgery or gastric decompression by suction.

When either occult or gross bleeding occurs with acute ulcer, this program need be altered little, if any, except to withhold feedings temporarily when the hemorrhage is sufficiently brisk to produce nausea and vomiting. When nausea and vomiting are not associated with hemorrhage of peptic ulcer, feedings judiciously given are helpful. This fact has been clearly established by Meulengracht.[13]

Quiescent Ulcer and Long-term Prophylaxis.—By the time the ulcer has become thoroughly asymptomatic, the individual should have established a satisfactory eating pattern, with regard to timing, quality, and quantity of food ingested. He should be encouraged to follow this pattern faithfully for an indefinite period. The physician should recognize that rigid, elaborate dietary programs have definite limitations when used for the purpose of minimizing recurrence and complications of ulcer activity. Furthermore, even the most determined patient will tire of and cease to follow a program that is too austere. It is wise to temper enthusiasm for dietary measures with a proper regard for what may be achieved thereby and for the ability of the patient to cooperate.

Miller [10a] has amply demonstrated that the traditional, ultraconservative prohibitions are of no importance for long-term prophylaxis. If the patient will eat temperately, regularly, and frequently under tranquil emotional and physical circumstances, he will attain most of the benefit that can be gained through dietary measures in the control of his ulcer. The judicious choice of a wide range of foods and the establishment of regular eating habits have psychological as well as physiological advantages. Insistence upon picayune selections and uncompromising prohibitions have no place in dietary management of peptic ulcer. In this connection a careful analysis of the patient's own previous experience with specific food tolerances is in order and extremely helpful in planning the diet. Obviously, food intolerances either unrelated to or related to peptic ulcer are to be vigorously avoided.

Factors Supporting a Liberal Ulcer Diet

In the past, certain foods were customarily excluded from ulcer diets because they were believed to irritate the gastric mucosa. Onions, garlic, turnips, parsnips, radishes, mustard, pickles, and all varieties of condiments are examples of these foods. Wolf [14] fed various foods, including those that were highly seasoned, to his fistulous subject whose stomach and duodenum were normal and to a second subject having a gastric fistula and an active duodenal ulcer. No evidence of irritation of the gastric mucosa appeared in either subject. Several chemicals, including strong condiments, were applied directly through the fistulas to the gastric mucosa of these two subjects and at the same time to the skin of their forearms. The local reactions in the gastric mucosa of these subjects were less impressive than the cutaneous reactions.

These "indigestible" ingredients of the diet probably are indigestible without relation to the presence or absence of ulcer because of specific food intolerances and their influence on motor and secretory function in a given individual. Thus, whether or not a food will be tolerated well by a patient with peptic ulcer in order to be included in the diet is best determined by trial. "Roughage" is another time-honored prohibition in the diet for the patient with peptic ulcer. It is highly improbable that "coarse" or "rough" foods, such as fruit skins, lettuce, cabbage, kale, nuts, celery, and endive when subjected to proper mastication or mixture with saliva, could ever actually traumatize a peptic ulcer. The emphasis, therefore, should be placed upon the proper preparation of food for gastric digestion. Ordinarily this is done satisfactorily in the mouth by mastication and mixture with saliva. Only when the teeth are poor or absent is artificial grinding or pureeing necessary.

Wolf [14] states, "As far as diet is concerned, it is evidently important to provide feedings that are frequent enough so that the stomach will not remain empty and it is also important that these feedings contain milk and cream which do as well at neutralizing and inhibiting gastric function as can be done. The most pertinent steps in the management of patients with peptic ulcer are concerned with a consideration of the person in the patient, including attempts to help him deal more constructively with problems and challenges in his day-to-day life. Certainly, before prescribing limitations to the diets of persons with peptic ulcer, we need better evidence that ordinary foods are either stimulating or irritating to the stomach." These observations by Wolf have given experimental support to proposals to liberalize the diet prescribed in the treatment of the peptic ulcer.

Summary

It appears that much of the rigid ritualism of the conventional dietary regimen is unnecessary for the satisfactory management of peptic ulcer. However, the discipline imposed by the requirements or regularity and moderation in eating is, in itself, of considerable value. This is especially true if such habits help to bring more peaceful organization to the disorganized and emotionally distraught person. A temperate and common sense approach to the diet prescriptions should provide for the essential nutritional and acid-reducing features, without making the diet an end unto itself or the patient a dietary cripple. With such an approach the physician can select for the patient with peptic ulcer those features of a conventional regimen that are useful. At the same time he can maintain healthy skepticism and avoid undesirable results of dietary nihilism.

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THE JOURNAL
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PRESIDENT EISENHOWER'S ATLANTIC CITY ADDRESS

FOR the first time in the 112 years of its existence, the American Medical Association was honored at the Annual Meeting in June by the participation of the President of the United States in its program. Mr. Eisenhower came to Atlantic City by plane Tuesday afternoon. He attended a small reception given by officials of the Association, then went to the Auditorium, where the inaugural ceremony of the Association was held. The President was present on the stage throughout the inauguration ceremony, following which he addressed an audience of more than 5,000 people within the Ballroom and, by loud-speaker, hundreds of others who gathered about on the Boardwalk. The President's address was heard also on television and on the radio.

President Eisenhower stated that the medical profession is steadily promoting better health among our people, whether it involves healing the sick, guarding the public against quackery, evaluating drugs, or helping to maintain high hospital standards. He reviewed the outstanding advances in the control and treatment of various diseases and noted the important part taken in them by the nursing profession and the hospitals. These advances, he said, are an inevitable reflection of American life. Better food, better sanitation, higher housing standards, better water supplies, and vastly extended education are factors that underscore the intimate link between an expanding economy and high standards of medical and health care. However, as our bodies must be vigorous, so must our economy. The President likened the relationship between a balanced diet and a balanced budget. Habitual violation of the requirements of a balanced diet can lead to ruined health, and to deliberately unbalance the federal budget in time of huge indebtedness and rapidly increasing prosperity can bring about an enfeebled economy. The choice is ours, he said, and we must act with clear mind and resolution in either case. The medical profession, which has a vital interest in preventing inflation, certainly wants to provide its services for a fee within range of what people can reasonably pay. The President said that, if the time ever comes when large numbers of our citizens turn primarily to the government for assistance in what ought to remain a private arrangement between doctor and patient, then we shall all have suffered a great loss.

But progress in medical science brings forth in itself new problems. The President then referred to the increasing number of our people 65 years of age or over who live largely on fixed retirement income represented in pensions, insurance policies, and savings. Inflation to this large group takes bread out of their mouths, clothes off their backs, and limits their access to medical care. The President was gratified to learn that the American Medical Association has embarked on an all inclusive program to re-orient our thinking about the place of older citizens in modern society and to help them meet their health care needs.

As civilization expands, many other challenges to medicine and to society arise. We are constantly called on, the President pointed out, for new assessment of our environment, imagination, and effort to force and prevent or to recognize and conquer these changes, among which are the problem of the neuroses, the rising curve of highway deaths and injuries, and new health hazards in the form of occupational diseases. Progress must lead also to the mastery not only of the newer threats to health but of such age-old scourges as cancer and diseases of the heart and mind and of the central nervous system.

In closing, President Eisenhower said that peace and ennoblement of the human spirit are the common aims of free societies and that we shall one day establish a world community of peace-loving nations. In bringing about this happy result, he said, no one can or will do more than the doctors of medicine.

SECOND WORLD CONFERENCE ON MEDICAL EDUCATION

The Second World Conference on Medical Education, which will convene in Chicago this year during the week of August 30-September 4, promises to be an interesting and valuable experience for those who attend and participate. Its general theme, "Medicine—A Lifelong Study," will deal with the challenges confronted in various parts of the world by education beyond completion of medical school studies. The four areas on which the conference will focus attention will include (1) basic clinical training for all physicians, (2) advanced education for general and specialty practice, (3) the development of teachers and investigators, and (4) continuing medical education.

Physicians and other medical educators from many nations throughout the world will be exchanging data on organization of curricula and methods of instruction. To facilitate this intercommunication, all of the conference sessions will be conducted with simultaneous translations of addresses and discussions into English, French, and Spanish, since all participants will be fluent in one or more of these three languages.

In addition to being of interest to those directly concerned with education in medical schools and associated teaching hospitals, this Second World Conference on Medical Education should hold special interest for hospital administrators, directors of education in hospitals, members of specialty boards, and state licensing boards. The conference should make it possible for such persons to discuss matters of mutual interest and concern. It will afford opportunities for better understanding of medical education abroad on the part of those who will be working with graduates of foreign medical schools who seek advanced training in the United States.

A résumé of the program of the Second World Conference on Medical Education appears on pages 1077-1078 of this issue of The Journal. In view of the broad interest which this conference will have, it is suggested that those who desire to attend arrange for their reservations (Conference Headquarters, Palmer House, Chicago) as early as possible. Programs and additional information may be obtained by communicating with Dr. Louis H. Bauer, Secretary-General, World Medical Association, 10 Columbus Circle, New York City.

MEDICAL MUSEUMS CAN BE HELPFUL TO PHYSICIANS

The busy physician is being reminded today more and more to remember that he is a teacher as well as a healer so far as his patients are concerned. It is no longer sufficient to advise a patient that he has a certain disease. Time must be spent with every patient to provide anatomic and pathological orientation. This has its rewards, as physicians discover from time to time that patients seek other advice "because the doctor didn't explain what was wrong." There are valuable educational sources available about which many physicians may be unaware. Reference is made to the fairly numerous health museums, the modern, refined versions of earlier "chambers of horror" by which lay visitors were frightened and often misinformed.

Vastly improved techniques of presentation, with extensive use of mechanized models, have contributed to better health understanding on the part of the public. Such exhibits serve to clarify the problems of normal physiological functions of the human body and thus to help laymen understand what abnormality is involved when disease strikes.

In a discussion of the genesis and development of health museums,[1] Gebhard, a pioneer in this field, notes that the oldest medical museum in the United States was founded at Charles-Town, S. C., by two physicians. Currently, medical societies have displayed commendable activity in initiating and supporting new medical museums.

Physicians will do well to encourage the educational support provided by health museums. They provide education at the important level of normal body functions, and so make the task of explaining abnormalities easier.

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ORGANIZATION SECTION

HIGHLIGHTS OF ATLANTIC CITY MEETING

The following is a summary of highlights of the 108th Annual Meeting of the American Medical Association, with special emphasis on actions of the House of Delegates. Future issues of THE JOURNAL *will carry an abstract of the proceedings which eventually will be presented fully in pamphlet form.*

After several transitional years of socioeconomic awareness leading to fuller recognition of responsibility, the typical American physician is now accepting a broad role in helping to lead his fellow citizens toward total personal well-being—but he is determined to do this in a manner emphasizing the soundest principles of medical philosophy.

Such a portrayal of today's doctor was indicated June 8-11 when his representative A. M. A. House of Delegates took decisive policy actions for positive relationships with medical care plans and with the osteopathic profession, reaffirmed its opposition to compulsory Social Security coverage of self-employed physicians, and enunciated broad goals for preparing the family physician of tomorrow.

The 208 delegates considered a total of 37 resolutions. Scientific sessions and exhibits in the giant convention hall and nearby hotels attracted 32,882 persons, including 13,143 physicians and 19,739 guests, exhibitors, medical students, nurses, and technicians.

By a vote of 122 to 81, the House at its final session chose Dr. E. Vincent Askey of Los Angeles as President-elect over Dr. George F. Lull of Chicago, former General Manager of the A. M. A. and now president of the American Medical Education Foundation. The California surgeon, who will become A. M. A. President next June in Miami Beach, relinquished his role of Speaker to Dr. Norman Welch of Boston. Dr. Milford O. Rouse of Dallas was elected Vice-Speaker. The new Vice-President is Dr. John Stanley Kenney of New York City. Two members of the Board of Trustees were re-elected: Dr. R. B. Robins of Camden, Ark., and Dr. Hugh Hussey Jr. of Washington, D. C. Elected to a five-year term on the board for the first time was Dr. Percy E. Hopkins of Chicago. He replaces Dr. W. Linwood Ball of Richmond, Va., who was appointed after the death of Dr. Warren Furey of Chicago. Later, the trustees re-elected Drs. Leonard Larson and Julian Price as Chairman and Vice-Chairman, respectively, of the board.

Atlantic City's famed beach lured many physicians and their guests, as almost perfect weather blessed the visitors. Hotel swimming pools were also well populated, and the sweep of the boardwalk lined with shops and amusements provided continual entertainment.

Social highlight of the A. M. A. session was the inaugural ceremony and ball when Dr. Louis M. Orr of Orlando, Fla., succeeded Dr. Gunnar Gundersen of La Crosse, Wis., as President of the Association. The guest of honor at this ceremony was Dwight D. Eisenhower, the first United States President ever to address an A. M. A. Annual or Clinical Meeting. He called on American physicians to protect the private arrangement between doctor and patient, and told the overflow audience of more than 5,000, "If the time ever comes when large numbers of our citizens turn primarily to the government for assistance in what ought to remain a private arrangement between doctor and patient, then we shall all have suffered a great loss." President Eisenhower also complimented the profession on its "all-inclusive program to reorient our thinking about the place of elder citizens in modern society and to help them meet their health care needs."

In his inaugural speech Dr. Orr urged his colleagues to help maintain the freedom which has inspired medical progress through the years. He said, "You must defend the unfettered, inquiring mind, for medical progress depends upon the relentless quest for truth by minds that are free."

The new A. M. A. President's first official act was to award the Distinguished Service Award for 1959 to Dr. Michael De Bakey, who was chosen by the House of Delegates from a field of three candidates including Dr. Jonas Salk of Pittsburgh and Dr. Shields Warren of Boston. Dr. De Bakey, of Houston, is best known as a research surgeon. He is noted for his contributions to cardiovascular surgery and the use of arterial grafts, including plastic substitutes for diseased portions.

Medical Care Plans

The much debated part 1 of the Commission on Medical Care Plans report was received by the House "for information only," but the Delegates adopted 36 of the 38 recommendations which accompanied it, as a climax of three and one-half years of study. The House at the same time accepted a special reference committee's rewording of three other recommendations relating to miscellaneous and unclassified plans.

The House accepted two of the Commission's recommendations regarding free choice of physician and altered a third, after noting that such choice is already facing restriction. This was the first time that the House has adopted statements attempting to define free choice. One portion of the reference committee report as adopted by the House stated: "In any discussion of free choice, consideration must be accorded to the limitation listed by the Commission and to the qualifying limitations cited by the constituent medical associations. These factors represent limitations of free choice which patients have accepted voluntarily or which have been imposed upon them and which have been condoned by the medical profession. These restrictions on free choice of physician are conditions existing today here and now, notwithstanding any policy implied or expressed by the American Medical Association."

The free choice recommendations accepted were:

—'Free choice of physician' is an important factor in the provision of good medical care. In order that the principle of 'free choice of physician' be maintained and fully implemented the medical profession should discharge more vigorously its self-imposed responsibility for assuring the competency of physicians' services and their provision at a cost which people can afford.

—Those who receive medical care benefits as a result of collective bargaining should have the widest possible choice from among medical care plans for the provision of such care.

The House noted that "many who testified at the reference committee hearings pointed out that if the medical profession had in the past discharged its responsibilities for assuring the competency of physicians, it would have prevented many of the problems existing today." Delegates did not adopt the Commission's third recommendation on free choice, but instead substituted the following:

"The American Medical Association believes that free choice of physician is the right of every individual and one which he should feel free to exercise as he chooses. Each individual should be accorded the privilege to select and change his physician at will or to select his preferred system of medical care, and the American Medical Association vigorously supports the right of the individual to choose between these alternatives."

The House adopted a series of recommendations on what medicine's relationships should be at all levels to closed-panel plans. Two other recommendations on this subject were changed to read:

—In an effort to decrease, or at least to prevent an increase in, the over-all cost of health care, study should be given to the removal of the requirement of hospital admission as the only condition under which payment of certain benefits will be made.

—Medical care plans should be encouraged to increase their efforts to provide health education and information concerning the coverage of their subscribers.

The House requested that the A. M. A. Division of Socioeconomic Activities "develop information which should be useful in the liaison between medical societies and third-party plans and in developing guides for the relationship between the medical profession and these third parties." While also urging that the A. M. A. Law Division draft a statement which would include all points a physician should consider in contracting with a plan, the House acknowledged a Commission conclusion that "there is no generally held opinion declaring that participation in closed-panel medical care plans would render a physician unethical."

Adopted without change from the Commission's report were its recommendations that:

—Medical profession-sponsored plans seek to extend their number and coverage as a deterrent to the future development of closed-panel plans.

—Efforts be made to resolve problems occurring in industrial health programs and to improve relationships between occupational health programs and practicing physicians.

—Local medical societies maintain close liaison with student health plans to the end that suitable health programs and education be developed and perfected.

Osteopathy

Basing its action on a report of the Judicial Council, the House adopted four recommendations on relationships between physicians and osteopaths. An indication of the interest in this subject is that the reference committee was forced to move its meeting to a larger hearing room in order to accommodate more than 125 participants and spectators. Subsequent debate in the House involved 21 delegates from 14 states and occupied 90 minutes of session. These are the House recommendations:

—All voluntary professional associations between doctors of medicine and those who practice a system of healing not based on scientific principles is unethical.

—Enactment of medical practice acts requiring all who practice as physicians and surgeons to meet the same qualifications, take the same examinations, and graduate from schools approved by the same agency should be encouraged by the constituent associations.

—It shall not be considered contrary to the Principles of Medical Ethics for doctors of medicine to teach students in an osteopathic college which is in the process of being converted into an approved medical school under the supervision of the A. M. A. Council on Medical Education and Hospitals. In a separate action concerning osteopathy, the House recommended that the A. M. A. representatives on the Joint Commission for the Accreditation of Hospitals suggest to that Commission that they inspect on request and consider for accreditation without prejudice those hospitals required by law to admit osteopathic physicians to their staff.

—A liaison committee should be appointed by the Board of Trustees to meet with representatives of the American Osteopathic Association, if mutually agreeable, to consider problems of common concern including interprofessional relationships on a national level.

Medical Education

The House approved the report of the Committee on Preparation for General Practice which urges a period of at least two years of formal hospital training after the attainment of the medical degree for doctors preparing for family practice. Most family physicians today began their practice after as little as one year of a rotating type of internship. The House recommended that new programs of preparation include:

—A minimum basic 18-month in-hospital training period to provide broad experience in the pediatric, diagnostic, therapeutic, psychiatric, preventive, and rehabilitation aspects of medicine.

—Regularly assigned periods of emergency room service and training in minor surgery.

—Provision for adequate opportunity for the study of outpatients.

The Committee's recommendation that training in obstetrics be a part of a six-month additional elective period and not be mandatory for those who do not anticipate an obstetric practice was adopted, but an Indiana delegation's resolution asking that such training be a requirement was referred to the Council on Medical Education and Hospitals for further consideration. The Committee on Preparation for General Practice includes representatives of the A. M. A. Council on Medical Education and Hospitals, the American Academy of General Practice, and the Association of American Medical Colleges. Its report noted: "The graduate program of two years in preparation for family practice should be planned and implemented as a unified whole with a maximum continuity of assignment in specific services."

Social Security, Other Actions

Three resolutions in favor of compulsory Social Security coverage for self-employed physicians and one calling for further consideration of the subject were disapproved by the House. A fifth resolution for the House to reaffirm its traditional stand in opposing compulsory inclusion was adopted. At a prior reference committee hearing 33 physicians spoke in favor of the A. M. A. stand while 5 opposed it.

The House also recognized the "apparent growing demand by physicians for economic security" and requested the Board of Trustees to investigate the possibilities of developing group insurance and retirement plans which could be made available to Association members.

The House of Delegates also:

—Called for all physicians to "endeavor to understand the socioeconomic aspects of the world in which they live, not because they are physicians or members of the American Medical Association but because they are citizens."

—Recommended that the 1962 Annual Meeting be held in Chicago during the week of June 11-15.

—Requested that the Board of Trustees study (1) the need for, (2) the method of selecting recipients of, and (3) the means of administering an A. M. A.-sponsored medical scholarship, loan program, or both, so that qualified students will not be deterred from entering medical school because of financial considerations.

—Congratulated the Joint A. M. A.-American Bar Association Committee on Narcotic Drugs on its "long, tedious, and fruitful work on the broad subject of narcotics," and urged continued study under "separate and already established councils of the A. M. A. and the ABA."

—Urged the establishment of a national commission to study and develop recommendations relating to trends in jury awards in cases involving personal injury. The House noted that a joint A. M. A.-ABA Liaison Committee has already done considerable work on this and related problems.

—Disapproved a resolution which would direct "that a reliable method be devised, under A. M. A. auspices, to evaluate and regularly report upon the acceptibility of foreign medical schools." The House decided that the intent of the resolution was neither practical nor necessary.

—Approved the inclusion of *Today's Health* and any one of the A. M. A. specialty journals as a benefit of dues-paying membership. Such members already receive THE JOURNAL and the *A. M. A. News* as a benefit.

—Recommended that state medical societies, where advisable, initiate legislative efforts to eliminate cancer quackery.

—Gave a vote of thanks to Dr. Joseph D. McCarthy of Omaha, who finished his term as chairman of the Council on Medical Service.

—Expressed appreciation for an outstanding disaster medicine program presented by the U. S. Army Medical Service in cooperation with the Council on National Defense in Atlantic City immediately prior to the Annual Meeting.

Related Activities

Others elected or re-elected during the session were:

Dr. J. M. Hutcheson of Richmond, Va., re-elected to the Judicial Council.

Dr. Charles T. Stone of Galveston elected and Dr. W. Andrew Bunten of Cheyenne, Wyo., re-elected to the Council on Medical Education and Hospitals.

Dr. Willard Wright of Williston, N. D., elected, and Dr. J. Lafe Ludwig of Los Angeles re-elected to the Council on Medical Service. Dr. Ludwig is the new chairman.

Dr. William Hyland of Grand Rapids, Mich., re-elected to the Council on Constitution and Bylaws.

Dr. Fred A. Humphrey of Fort Collins, Colo. elected as Chairman of the Council on Rural Health, succeeding Dr. F. S. Crockett of Lafayette, Ind., who remains a member.

Meeting at the same time as the A. M. A. in Atlantic City, the Woman's Auxiliary installed Mrs. Murphy Jr. of Canon City, Colo., whose exhibit Frank Gastineau of Indianapolis as new president, and named Mrs. William Mackersie of Detroit as president-elect.

America's younger generation of medical scientists were represented at the session by Kay Schuele of Memphis, with an exhibit on algae, and Martin was on the role of radioactive testosterone in hematopoiesis. Both are teen-agers, and were winners in the medical science division of the National Science Fair held in Philadelphia last month.

The choice of Atlantic City as the site of the Annual Meeting—called "the greatest medical show on earth"—made a medical Mecca of the area for the first two weeks of June. Held around the time of the Annual Meeting were sessions of more than 20 other medical and allied organizations.

SECOND WORLD CONFERENCE ON MEDICAL EDUCATION

PALMER HOUSE, CHICAGO, AUG. 30-SEPT. 4, 1959

THE PROGRAM

COLLABORATING ORGANIZATIONS

The World Health Organization
Council for International Organizations of Medical Sciences
International Association of Universities

PATRON

the Honorable Dwight D. Eisenhower
President of the United States
of America

OFFICERS

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Dr. Raymond B. Allen, Chancellor, University of California at Los Angeles (U. S. A.)

Deputy Presidents

Dr. Victor Johnson, Director of Mayo Foundation for Medical Education and Research, University of Minnesota Graduate School of Medicine (U. S. A.)

Dr. Roy F. Farquharson, Sir John and Lady Eaton Professor of Medicine, University of Toronto (Canada)

Vice-presidents

Section 1: Prof. Yoshio Kusama (Japan)
Dr. Gabriel Velazquez Palau (Colombia)
Section 2: Prof. Sir George Pickering (England)
Prof. Dr. D. P. Fuchsig (Austria)
Section 3: Prof. C. Heymans (Belgium)
Prof. Dr. V. R. Khanolkar (India)
Section 4: Prof. Dr. Alejandro Garreton Silva (Chile)
Dr. A. Soliman (Egypt)

Rapporteurs

Section 1: Dr. E. Hugh Luckey (U. S. A.)
Section 2: Dr. Oliver Cope (U. S. A.)
Section 3: Dr. W. Barry Wood Jr. (U. S. A.)
Section 4: Dr. S. S. B. Gilder (Canada)

The program, which will officially open with a full-day plenary session on Monday, Aug. 31, will be devoted to consideration of the general concept of "Medicine—A Lifelong Study." After this initial plenary session the program will be divided into four sections dealing with the following general areas of consideration:

Section 1: Basic Clinical Training for All Doctors
Section 2: Advanced Education for General and Specialty Practice
Section 3: The Development of Teachers and Investigators
Section 4: Continuing Medical Education

Physicians and other medical educators from nations throughout the world will participate in these section programs. To facilitate understanding and intercommunication, arrangements have been made for simultaneous translation into English, French, and Spanish, as all attending will be proficient in one or more of these languages. Over 120 speakers from more than 50 nations will address one of the plenary sessions or one of the section groups during the program.

The final day of the program, Sept. 4, 1959, will be devoted to reports from the sections and to a closing address on "Medicine—A Lifelong Study" to be delivered by Lord Cohen of Birkenhead.

The following material presents detailed information concerning the initial plenary session on Aug. 31 and a skeletal outline of the section sessions which will subsequently be conducted.

AUG. 31, 1959

Plenary Session

10:00 a. m. Opening Ceremonies
11:00 a. m. Presidential Address
Dr. Raymond B. Allen (U. S. A.)
11:40 a. m. Summarization of First World Conference on Medical Education
Prof. W. Melville Arnott (U. K.)
Prof. Ian Aird (U. K.)
2:30 p. m. International Cooperation in Postgraduate Education
Dr. E. Grzegorzewski (W. H. O.)
Dr. U. K. Shetls (India)
Dr. G. Monteiro (Malaya)
3:45 p. m. Value of Participation in Research as a Component in the Education of Doctors
Dr. Victor Johnson (U. S. A.)
Prof. R. F. Farquharson (Canada)
4:15 p. m. Discussion, chaired by Dr. Robert A. Moore (U. S. A.) and Dr. Maurice B. Visscher (U. S. A.)

Sept. 1, 1959

Morning

SECTION 1: BASIC CLINICAL TRAINING FOR ALL DOCTORS

Historical development of clinical experience before qualification, including methods of acquiring clinical experience, will be discussed. Included will be curriculum and methods of instruction on inpatient and outpatient services, as well as integration of essential portions of specialties in the major areas of medicine.

Conference and seminar methods will be compared to amphitheatre instruction.

SECTION 2: ADVANCED EDUCATION FOR GENERAL AND SPECIALTY PRACTICE

Training for general practice: the need for advanced training; faculty responsibility in this field; length and scope of advanced training; extrahospital experience; opportunities for such training.

Training for specialization: determination of specialties and subspecialties; length and scope of advanced-training; medical faculty responsibility for specialty training standards; opportunities for such training.

SECTION 3: THE DEVELOPMENT OF TEACHERS AND INVESTIGATORS

Problems of recruitment and factors influencing opportunities for careers in teaching and research; prestige; economics; educational traditions; procedures governing appointments and promotion; competitive examinations.

SECTION 4: CONTINUING MEDICAL EDUCATION

The objectives and problems of continuing medical education.

The administrative and organizational techniques useful in continuing medical education.

Intramural and inservice programs of continuing medical education.

Afternoon

During the afternoon, tours will be arranged for visits to the medical schools and hospitals in Chicago, and participants may visit the American Medical Association headquarters or other points of interest.

Sept. 2, 1959

Morning

SECTION 1: COMPLEMENTARY EXPERIENCE FOR MEDICAL STUDENTS

Socioeconomic aspects of life and their role in health and disease; limitations of traditional patterns in developing total patient care concept; experimental approaches in teaching social medicine; student research—an educational experience and a means of future academic recruitment.

SECTION 2: FORMAL COURSES IN ADVANCED TRAINING

Their place in advanced training for general practice; their place in advanced specialist training; recognition of advanced training through awards of postgraduate degrees.

The Place of Applied Basic Science in Advanced Training

Formal courses in applied basic sciences; hospital laboratory experience as a component in specialist training, research experience in the training of the specialist.

SECTION 3: EXPERIENCE BEFORE AWARDING THE QUALIFYING DEGREE

Research experience for candidates for qualifying degree in medicine; basic medical sciences curriculum without clinical training.

Fellowships and Assistantships as Economic Assistance from Government and Foundations

SECTION 4: EXTRAMURAL PROGRAMS

Visiting lecturers and organized teams from medical faculties and hospital centers; use of rural hospitals and community health centers; closed circuit television and radio broadcasts; library services; scientific journals; assemblies and demonstrations.

Afternoon

SECTION 1: BASIC CLINICAL TRAINING FOR ALL DOCTORS

Preceptorships for medical students: objectives; methods of preceptorship training; evaluation of merits.

Patterns and methods of full-time practical education before practice or specialization.

SECTION 2: ADVANCED EDUCATION FOR GENERAL AND SPECIALTY PRACTICE

Professional responsibility for patient care: progressive responsibility programs; supervisory techniques in advanced training.

The relative role of government, medical schools and the medical profession in identification, recognition, or certification of general practitioners and specialists.

Community resources as a field of advanced training.

SECTION 3: THE DEVELOPMENT OF TEACHERS AND INVESTIGATORS

Advanced teaching and research experience after professional qualification: international exchange programs; research opportunities; teaching experience; development and evaluation of teaching skills; post doctoral fellowships.

SECTION 4: CONTINUING MEDICAL EDUCATION

There will be demonstration and discussion of audio-visual aids.

Sept. 3, 1959

Morning

SECTION 1: BASIC CLINICAL TRAINING FOR ALL DOCTORS

Panel and open discussion.

SECTION 2: ADVANCED EDUCATION FOR GENERAL AND SPECIALTY PRACTICE

Panel and open discussion.

SECTION 3: THE DEVELOPMENT OF TEACHERS AND INVESTIGATORS

Panel and open discussion.

SECTION 4: CONTINUING MEDICAL EDUCATION

Panel and open discussion.

Afternoon

Again on Thursday afternoon tours will be arranged for visits to the medical schools and hospitals in Chicago, and participants may visit the American Medical Association headquarters or other points of interest.

Evening

Thursday evening the official conference dinner will be held. Tickets will be available at the registration desks.

It is hoped that many physicians and other medical educators from the United States will plan to attend this important conference to participate in the exchange of ideas and experiences with our colleagues from abroad. This should be of particular interest to hospital administrators and professional staff personnel who may desire to have an opportunity to confer with those most familiar with the educational background of some of the graduates of foreign medical schools.

Full details concerning the program may be obtained by communicating with Dr. Louis H. Bauer, Secretary-General, World Medical Association, 10 Columbus Circle, New York 19.

CLINICAL MEETING, DALLAS, DEC. 1-4, 1959

The Council on Scientific Assembly announces that the program for the Clinical Meeting in Dallas is rapidly taking shape. Dr. Everett C. Fox, general chairman of the local committee, is directing his attention to the clinical aspects of the meeting and its practical application to everyday medical practice. Dr. Charles D. Bussey, Dallas, has assembled an outstanding program of lectures, symposiums, panel discussions and breakfast meetings. Dr. John S. Chapman, Dallas, is working on the color television program which will include unique features. Mr. Ralph P. Creer, Chicago, is arranging a full three-day showing of the latest motion pictures.

Applications for space in the Scientific Exhibit at Dallas should be submitted by Aug. 1. Inquiries for application blanks for space or for other information should be addressed, as soon as possible, to the Secretary, Council on Scientific Assembly, American Medical Association, 535 N. Dearborn St., Chicago 10.

COUNCIL ON MEDICAL SERVICE

CHRONIC ILLNESS INFORMATION CENTER OF CLEVELAND

The Chronic Illness Information Center of Cleveland was established in March, 1955, as a department of the Welfare Federation in that city. Prior to this, requests for referral services and information on chronic illness facilities and services had been handled by a number of different agencies in Cleveland, among them the Benjamin Rose Institute (a philanthropic health and welfare agency for older persons), the Catholic Charities Bureau, County Welfare Department, Jewish Family Service Bureau, the Welfare Federation Community Information Service, and the Highland View Hospital for Chronic Diseases. Duplication and overlapping of functions often resulted in confusion and inadequate services. In recognition of the need for coordination of services and pooling of information, the chairman of the Welfare Federation's Committee on the Chronically Ill appointed a subcommittee of persons from the various organizations furnishing service to the chronically ill to consider the need for a central information-gathering, counseling, and referral agency. The subcommittee, after its study, unanimously recommended establishing a central information service in Cleveland.

A subsequent committee of lay and professional persons was appointed to draft the organizational details of the center and to develop its specific functions and purposes, which were established (1) to give patients and other persons direction and advice regarding facilities for long-term care, to guide the individual patient to the proper facility as his needs change, and to serve as a focal point for closer cooperation between agencies in service to the individual patient; (2) to centralize the consultation and referral services being given in part by several different agencies, thereby eliminating duplication and promoting the most efficient use of facilities available; (3) to continuously evaluate community resources and unmet needs through systematic inquiries, follow-up of patients referred, and contacts with other agencies serving the chronically ill and to refer to the Welfare Federation Committee on the Chronically Ill any gaps in service which require community action; (4) to serve in a consultant capacity to the operators of nursing and boarding homes and to persons planning to establish such facilities in regard to improved standards of care; and (5) to cooperate with other community agencies in promoting the development and expansion of needed facilities and services and in fostering an enlightened public attitude toward the problems of long-term illness.

The information center is still operating as a department of the Cleveland Welfare Federation and receives financial support from the federation, the Benjamin Rose Institute, and a private source. In addition, the Cleveland City Division of health has assigned a public health nurse to the staff. The Academy of Medicine of Cleveland contributed to the support of the center during its first three years of operation.

Organization and Operation

The information center occupies office space in the Community Service Building, which houses most of the Welfare Federation departments. Office staff consists of a director, a public health nurse, and a secretary. The center operates under the supervision and guidance of an advisory board composed of professional and lay persons representing the Cleveland Academy of Medicine; the Visiting Nurse Association; Catholic Charities; Jewish Community Federation; various city, county, and state health and welfare agencies; special health organizations; private casework agencies; general and chronic disease hospitals; and hospital social service departments. This advisory board, under chairmanship of a physician, acts as a liaison group between the center and the Welfare Federation's Committee on the Chronically Ill. Although each has its own staff, the work of the Committee on the Chronically Ill and that of the information center is well integrated.

The Committee on the Chronically Ill is directed by the same executive secretary as the Committee on Older Persons because of the many overlapping needs of the chronically ill and the aging. Its functions are the planning and coordination of community services relating to chronic illness in the light of data gathered by the information center in its work with individual patients and facilities.

The director of the center is a medical social worker, employed on a part-time basis. Her duties, in addition to over-all administration and supervision of staff, include providing information, counseling, and referral services to patients or other persons in regard to facilities for care; contact with agencies providing direct services in regard to their policies and procedures; maintenance of statistics on services provided; and intepretation of the pro-

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This is part of a series of articles, prepared by the Council on Medical Service, on chronic illness information centers in various parts of the United States.

gram to those providing the services and to other appropriate groups in the community. The director also visits and consults with nursing home operators and those planning such facilities in regard to standards of care and cooperates with the state licensing division in improving standards of care.

The public health nurse was assigned from the Cleveland Division of Health to work with the information center. She spends half of her time in the information center office where her work includes counseling and referral of persons seeking facilities for care and liaison with the division of health and other city and state agencies concerned with licensing and inspection of nursing homes. She also acts as a consultant in standards of care to nursing home operators and persons planning new facilities. Her duties as a consultant to operators of nursing homes and homes for the aged are performed directly as a program of the division of health, but as such are also in line with the purposes of the information center.

The secretary handles most of the clerical-administrative detail in the office. She serves as receptionist and telephone operator, receives all requests for information—the majority of which come by telephone—and obtains identifying information before routing the request to the professional staff. She also makes many of the follow-up calls on inquiries.

TABLE 1.—*Persons Served in 1955, 1956, and 1957*

Year	Patients, No.		Other, No.‡
	New*	Recall†	
1955	744	7	479
1956	884	65	467
1957	824	63	582

* Patients known to center for first time.
† Patients who have received previous service from center.
‡ Requests for service not related to specific patient.

Files and records maintained in the center include a detailed individual request form on each patient for whom service is sought, giving diagnosis and health status, referral source, socioeconomic information, and other data; a monthly numerical check sheet summarizing data on all requests for service during that period; closed case records filed by type of disposition or placement; and yearly reports.

The center also maintains detailed records on chronic illness facilities and services in the community. These include an individual record sheet for each nursing home, boarding home, or home for the aged in Cleveland and card files on persons or groups wishing to establish these facilities, persons providing care for one or two patients only, hospitals, special health organizations, and other health and welfare agencies. Records are also kept of various institutes, conferences, and meetings on chronic illness, along with a general source file of information on the subject.

Services to Patients

Patients requesting help from the center are accepted for service without any detailed investigative procedures, except that any other agency which has had prior contact with a patient is contacted for clearance and pertinent data. The center has not carried on any intensive publicity campaign directed toward either patients or community agencies, although health and welfare agencies were informed of its functions. This policy was established at the beginning, when the advisory board felt that widespread publicity should wait until the center was well established and community facilities were more readily available in order to avoid disappointment when no ready solution could be suggested for a number of persons seeking service. However there was some newspaper publicity at the time of the center's opening. A brochure describing the center was published by the City Division of Health and the center, for general distribution, and articles have appeared in local medical and other professional journals from time to time. Other channels of information have been talks by center personnel to various lay and professional groups, participation in state and local conferences and institutes, one television program devoted to the chronically ill, and mention of the center's services in radio programs on health.

The center routinely follows up every request for services. Anywhere from 60 to 90 days after the original contact, the family or other person who referred the patient to the center is called to see what arrangements were worked out. To date, a solution which is satisfactory in varying degrees has been reported in about 60% of the cases.

The average inquiry to the center usually involves about eight calls—the original contact, calls from other members of the family, calls to physicians and social agencies, and the follow-up. In some cases, the number of calls has been as high as 20 to 30, and the center feels that this, among other factors, reflects a lack of coordination among the different agencies serving a particular person. Patients are referred to the center by their families, relatives, friends, hospitals, private physicians, public and private welfare agencies, attorneys and guardians, the clergy, and industry.

The number of patients and other persons seeking help at the center during a year's time has stabilized at around 1,200 to 1,400 during the first three years of its operation. During the calendar year 1957, a total of 1,469 patients or other persons contacted the center for service, an increase of only 3.7% over 1956. Sixty-three of these requests were recall cases or patients who had previously contacted the center for service, and 582 were requests for service not related to an individual patient. Table 1 shows the number of requests for service for the latest three years data was available, divided according to new and recall patients, and other requests not concerned with a specific patient. The large number of contacts in this last category is partly due to requests for information by the personnel of health and welfare agencies who were contacted by the center when it was compiling a directory of services for the chronically ill.

Of the 824 new patients referred to the center in 1957, more than 80% were 60 years of age or older, and the average patient age has been close to 75. About twice as many women as men have been referred to the center, a rate which has been relatively constant over the years of operation until the later part of 1957, when there was an increase in male patients. About 63% of the patients were widowed or single, 27% lived alone, and 38% lived with friends or relatives. Over the years of operation an increasing proportion of semiambulatory patients have been referred to the center, with a corresponding decrease in fully ambulatory and bedfast patients. There has also been some change upward in patients' ability to pay for frequently requested services. There was an increase of two-thirds in those able to pay $300 or more per month and a one-third increase in those able to pay from $200 to $300. There was no significant change in the number able to pay $176 to $200 a month and a decrease in those who could pay $100 to $175 per month.

Table 2.—*Characteristics of New Patients Referred to Center in 1957*

	Patients, No.
Sex	
Male	337
Female	479
Not recorded	8
Age	
<20	3
21-40	29
41-60	91
>60	679
Not recorded	22
Marital status	
Married	207
Single	124
Widowed	395
Divorced or separated	37
Not recorded	61
Living arrangements	
Alone	222
With spouse	174
With relatives or friends	310
Boarding or nursing home	57
Hospital	21
Other institution	1
Not recorded	39
Degree of Disability	
Ambulatory	275
Semiambulatory	339
Bedfast	152
Not recorded	58

	Patients, No.
Method of contacting center*	
Phone	770
Letter	161
In person	45
Main source of income or support of persons referred†	
Spouse	69
Other relatives and/or friends	161
OAA	29
OAA plus relatives, OASI, etc.	27
Other public welfare	23
Pensions (retirement, veterans, etc.)	99
OASI plus savings, relatives, etc.	186
Income from business, employment, or rentals	41
Savings only	52
Capital assets, convertible property	68
Disability and employment insurance	23
No income	1
Not recorded (source unknown)	45

* Includes more than one contact by some patients.

† Most of the requests are for financially independent persons: plans for financially dependent are made by public assistance agencies.

Table 2 shows the characteristics of patients newly referred to the center during 1957, by age, degree of disability, living arrangements, financial status, and other factors.

Needs of Patients

During the calendar year 1957, requests for nursing home, boarding home, or other institutional care accounted for 76% of all needs for service among newly referred patients. The next most frequent requests were for consultation with other agencies and individuals regarding care, for information on a specific facility, and for consultation on standards of care from persons planning new nursing or boarding homes. Table 3 shows the nature of requests for service received by the center during 1957, divided according to new and recall contacts.

Table 3.—*Nature of Requests in 1957*

	New Cases	Recalls*	Total
Nursing home, boarding home, institution	627	38	665
Housekeeper, attendant, etc.	27	14	41
Information re facilities and Resources			
Sheltered or home employment	5	1	6
Financial assistance	64	8	72
(Referred to agencies: 31 new, 3 recalls)	34		
Wheel chairs, hospital beds, etc.	5	0	5
Rehabilitation services	18	1	19
Medical & Dental care	145	8	153
Free or cheaper medicine	8		8
Housing	49	0	49
Transportation to clinics	2		2
Recreation and companionship	52	15	67
Day care (custodial)	5	1	6
Restaurants serving special diets	0	0	0
Miscellaneous procedures, legal advice, camp, etc.	114	4	118
Information re a specific facility	111	23	134
Consultation with:			
Agencies' staffs, clergy, lawyers, personnel directors in industry, etc. (where these persons take responsibility for advising regarding care)	212	0	212
Prospective operators of nursing and boarding homes	93	0	93
Counseling, where center assumes responsibility for providing information, advice, and referral services for care of individual patients (Frequently involves consultation with physicians, agencies, and others concerned)	675	0	675
Total†	824	63	887

* Persons previously receiving service from agency.

† All cases reported are kept open for a minimum of 60 days when a follow-up call is made. If additional service is needed the case is continued as long as necessary. No case is closed until a decision has been made regarding the care of the patient. Cases listed as recalls are those which were closed after a solution had been reached and a change of situation brought further request for service. During the time cases are kept open there may be frequent requests for additional information. While these are indicated on the case history, no separate count is kept of them.

Requests for service to patients come to the center from the patients themselves and their families, hospitals, friends, private physicians, private and public welfare agencies, clergy, attorneys, guardians, and industry, in roughly that order of frequency.

The community facilities and services to which patients are most frequently referred have been nursing and boarding homes. Other referrals have been to homes for the aged, physicians, private casework organizations, public assistance agencies, the Visiting Nurse Association, special health organizations, public and private employment agencies handling nursing and/or attendant services, agencies providing homemaker service, chronic hospitals (through physicians), the Legal Aid Society, probate court, and agencies providing counseling on rehabilitation services, housing, or recreational programs.

Problems and Developments

In some three and one-half years of counseling, referral, and follow-up with patients, and contacts with other community agencies, the center has brought out into clearer focus a number of problems and future areas for action in meeting the needs of aged and chronically ill persons in Cleveland. The major problems yet to be resolved are summarized by the center as follows: (1) greater coordination and integration of service among all agencies serving the chronically ill and more flexibility in policies and services, particularly between general and chronic disease hospitals regarding their discharge policies; (2) additional nursing home facilities for male patients and for other specific groups such as Negroes of both sexes, persons with arrested cases of tuberculosis, younger persons from 18 to 30 and 30 to 50, physically disabled persons who are also alcoholic, mentally ill convalescent patients, mentally retarded children under 6 years of age, persons able to pay from $350 to $500 a month for care, ambulatory patients who require mostly sheltered living, and "in between" senile patients who are severely confused but do not require care in a mental hospital; a need for improvement of services in nursing homes generally, including better integration with hospitals and the entire community program for the chronically ill; related problems such as adequacy of public assistance payments for nursing home care and stronger action by state and local agencies regarding unlicensed facilities; (3) additional social casework and counseling services geared to the many problems accompanying long-term illness, such as dwindling finances, family attitudes, living arrangements, and the psychological impact of long-term dependency; (4) financial assistance for marginal income persons who are ineligible for public assistance but are unable to meet the full costs of care themselves; (5) additional services for chronically ill patients at home, including housekeeping, "meals on wheels," friendly visiting, rehabilitation services, and recreational activities, ideally provided through an organized home care program; (6) expansion of recreational services for chronically ill or aging persons, including some day care centers, and a visiting recreational or diversional service for persons at home or in nursing homes; (7) a method for insuring continuity of medical and rehabilitation services, from the hospital through the nursing home to the patient's own home, with additional special facilities or services provided as needed; (8) housing facilities tailored to the income of disabled older persons who can still carry on independent living; (9) more public education regarding the facilities available and the additional services needed for the chronically ill; and (10) increased participation by private and public agencies, particularly the latter, in financing care for this group.

The progress which has been made in each of these specific areas is summarized by the center as follows:

1. A study of public health methods in Cleveland was made by the Cleveland Metropolitan Services Commission in 1957. Recommendations growing out of this survey include the merging of the Cleveland and other municipal and county health departments into a single agency and, pending such a merger, the appointment of a county coordinator for chronic illness and aging who would act as a deputy commissioner for all health departments (this position to be retained after the merger); strengthening the contacts between public agencies such as health departments and hospitals and private nursing homes to improve the scope and quality of services in the latter; and, finally, developing an over-all plan for the selective placement of persons needing long-term institutional care.

The Cleveland City Hospital has already been merged administratively with the Highland View Chronic Disease Hospital, and a similar step is being considered for the two county nursing homes. Great progress has been made in integrating the services of the general and chronic disease hospitals for patients with long-term illnesses. There are now sufficient hospital beds for such patients.

2. A number of nonprofit nursing homes and homes for the aged in Cleveland have or are planning to expand their facilities and scope of services. Specific projects include a new 150-bed nursing facility providing multitype services for both bed and ambulatory older persons under auspices of the Benjamin Rose Institute and integrated with its hospital and home-care services; the addition of 36 nursing-home beds and a rehabilitation unit to a Catholic home for the aged; a 39-bed wing for nursing care at the Lutheran Home for the Aged; the opening of a 26-bed facility for indigent terminal cancer patients and plans for expansion to a 100-bed facility; addition of 40 beds to the Jewish Convalescent Hospital; the addition of nursing home sections or wings to a number of homes for the aged; and tentative plans for a multiservice type nursing facility for Negro patients. There is proposed a 94-bed addition to one of the two county nursing homes. Since the information center began operation, licensed proprietary nursing home beds have increased from 910 to 1,210 in number. Some of these are homes with excellent standards; others do not have the quality of care desirable. The need for homes in the $300 to $500 bracket is rapidly being met. The Cleveland Center on Alcoholism is planning to develop a program for services to alcoholic patients in nursing homes.

Regarding the improvement of services in nursing homes, the information center, in addition to providing the consultation services of a public health nurse and a medical social worker to individual nursing homes, has cooperated with the state nursing home and county home associations in sponsoring two state-wide workshops at one of the state universities and two institutes at Western Reserve University, devoted to the care of older and chronically ill persons in institutions. The center also cooperates with the City Division of Health and the State Licensing Division in holding educational meetings for nursing home operators and on a committee for coordination of state and local licensing requirements, has arranged with individual operators for the consultant services of the welfare federation's nutritionist, and has developed record forms for exchange of medical information between nursing homes and hospitals' out-patient departments, in cooperation with the social service departments of the local hospitals. The information center is working with the Volunteer Bureau of the Welfare Federation to develop group activity programs and friendly visiting services for nursing home patients.

The center, the state licensing division, and local zoning and safety authorities are systematically obtaining information on any unlicensed nursing homes in operation and making efforts to either close or license these facilities.

3. A committee has been appointed by the Committee on the Chronically Ill to study the need and possible methods for providing additional casework services for chronically ill persons.

4. The information center and other departments of the Welfare Federation have been working with public assistance officials to promote financial aid to the marginal income group. The maximums paid by both Aid for the Aged and the County Welfare Department are presently inadequate for nursing home care, and there are continuing efforts to have these amounts raised.

5. In regard to organized home services for chronically ill and older persons, two agencies in Cleveland, the Visiting Nurse Association and the Mount Sinai Hospital, are planning to establish home care programs. The Benjamin Rose Institute is continuing its home care program, which is limited to older persons served by the institute. The Jewish Family Service Association has developed a program of homemaker-personal care services provided under the supervision of the patient's private physician and the Visiting Nurse Association and has expanded its friendly visitor service for older persons to include those in nursing homes.

6. Different groups and agencies in the community continue to develop and expand recreational programs for the aged and chronically ill. The two Jewish homes for the aged have these services in their day care programs, and the Golden Age Center, established in 1955, provides services of this type for many older persons who have some chronic disability. A group recreational worker has been employed jointly by the welfare federation and the Benjamin Rose Institute to set up programs in four homes for the aged, and the Catholic Charities Bureau has also provided such services in three of its homes.

7. The Visiting Nurse Association has added a physical therapist to its staff, to instruct nursing personnel in rehabilitation procedures which can be given in the patient's own home. The welfare federation and the health council have a joint committee on rehabilitation which considers the individual patients needs, the services available, and their use. The committee sponsored a research study in this area which is being conducted by the county chronic disease hospital.

8. A special Committee on Housing for Older Persons has been appointed by the welfare federation, and a one-day conference on this subject has been held. This committee has drawn up plans for establishing a 164-suite apartment-hotel unit for middle-income older persons who need semiprotective living arrangements with some supportive services and supervision. Western Reserve University will conduct a research study of this project, under a grant from the Ford Foundation.

9. Although there has been no formal program of public education regarding chronic illness, a number of individual activities and projects have contributed to this end since the center's inception.

In addition to the various activities mentioned previously, the information center has compiled and distributed a 108-page Directory of Services for the Chronically Ill of Greater Cleveland. The directory, published jointly by the Welfare Federation's Committee of Special Health Organizations and the Cleveland Academy of Medicine, lists over 200 Cleveland health and welfare agencies providing services to the chronically ill and gives information on eligibility requirements, fees, hours, areas served, and referral procedures for each. The Committee on Older Persons and the Occupational Planning Committee of the Welfare Federation has also published a directory giving the services available in the community for older persons. The Committee on Older Persons cosponsors an annual conference on aging with the Junior League, and programs on chronic illness have also been conducted at three of the recent annual health and welfare institutes.

Finally, the staff of the information center and that of the Welfare Federation Committee on Chronically Ill continue to give talks, prepare exhibits, and plan programs on the chronically ill and their care, directed toward lay and professional groups in the community.

Because of the division of the functions of planning and coordinating community care for the chronically ill (which are the responsibility of the Committee on the Chronically Ill) and those of direct information, consultation and referral services to individuals (which are the responsibility of the Chronic Illness Information Center), the center does not direct, conduct, or sponsor by itself a great many of the community programs or activities previously mentioned but cooperates with the Committee on the Chronically Ill and other organizations and agencies in the community in providing them.

MEDICAL NEWS

HAWAII

State Medical Election.—The following were elected at the annual meeting of the Hawaii Medical Association: president, Dr. Toru Nishigaya; president-elect, Dr. Edward F. Cushnie; treasurer, Dr. Frederick L. Giles; A. M. A. delegate, Dr. Harry L. Arnold Jr.; and A. M. A. alternate delegate, Dr. Richard D. Moore. All are from Honolulu.

ILLINOIS

Chicago

University News.—Dr. Ake Hanngren, of the University of Stockholm Karolinska Hospital, who specializes in the study and treatment of tuberculosis and chest diseases, joined University of Chicago researchers in the department of pharmacology in using radioactive isotopes in a study of new anti-tuberculosis drugs. Dr. Hanngren's visit is sponsored by the Trygger Foundation of the Swedish Medical Association. He plans to remain in the U. S. for about six months.——Mr. David R. Corbett, San Francisco, recently financial vice-president, Curtiss Candy Company, was made vice-president in charge of business administration for the Chicago Medical School.

MICHIGAN

Dr. Furstenberg Retires.—Dr. Albert C. Furstenberg, dean of the University of Michigan Medical School, Ann Arbor, will retire July 1. Dr. Furstenberg received his M.D. degree at the University of Michigan in 1915, served in the Medical Corps in World War I, and returned to the campus in 1918 to begin specializing in the field of otolaryngology. He rose to the rank of professor in 1932 and chairman of the department. Appointed dean in 1935, he is the seventh administrative head of the U-M Medical School since its founding in 1850, but only the fourth to carry the title of "Dean." Dr. Furstenberg will continue in private practice.

Association of the Professions.—Dr. George W. Slagle, taking office as president of the Michigan State Medical Society in 1957 urged the House of Delegates of his society to take action in promoting an association of the professions "to the end that all professions might work together for the mutual benefit of all professions and the clients they served." The House of Delegates endorsed the idea and later that year the MSMS Council made funds available for organizational groundwork and instructed their Public Relations Counsel to proceed in the organization of such an association. The ideas were presented to the boards of the four other state societies: the Michigan Society of Architects, the Michigan Society of Professional Engineers, the Michigan State Dental Association, and the State Bar of Michigan. On July 21, 1958, leaders of these societies met at Michigan State University to formulate plans. They adjourned united in a statement of purposes for a new organization to be known as the Michigan Association of the Professions (MAP). They outlined possible services in legislation, education, public relations, and business techniques. A common letter and a questionnaire were mailed to the more than 21,000 members of the five state societies. Most of the members (4 to 1) were of the opinion that an association of the professions such as proposed could render a valuable service to their profession and that their own state professional society should join. Plans included a membership that would be made up of all professional people legally registered, certified or licensed or otherwise qualified as a member of the medical, dental, legal, architectural, and engineering professions and such other professions as might be subsequently admitted. On Dec. 1, 1958, articles of incorporation as a nonprofit organization, under the laws of the State of Michigan, were accepted by the Michigan Corporation and Securities Commission. Dr. William M. LeFevre is president of MAP. The main purpose of the organization is to function as an active organization developing its entire efforts to the economic, political, social, and public relations common to all professions.

MONTANA

Dr. Gordon Goes to India.—Dr. Wayne Gordon, Billings, announced that he will discontinue the practice of internal medicine in association with the Billings Clinic and will move to India to accept an appointment as associate professor of medicine at Christian Medical College in Vellore. Dr. Gordon has served as a member of the State Board of Medical Examiners and as Governor for Montana of the American College of Physicians.

NEBRASKA

Dr. Gillick Goes to California.—Dr. Frederick G. Gillick resigned as dean of the Creighton School of Medicine, Omaha, effective June 30. He also resigned as chief of staff for St. Joseph's Hospital. He

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Physicians are invited to send to this department items of news of general interest, for example, those relating to society activities, new hospitals, education, and public health. Programs should be received at least three weeks before the date of meeting.

will take a position as director of medical institutions for the County of Santa Clara, Calif., about Aug. 1. Dr. Gillick joined the Creighton staff in September, 1951, as dean. He holds fellowships in the American Public Health Association, the American College of Physicians, the American College of Preventive Medicine, and the American College of Cardiology. He is also a member of the Medical Advisory Committee of the Catholic Hospital Association.

NEW JERSEY

Society News.—The New Jersey Dermatological Society held its annual meeting May 12. The following members were installed as officers for 1959-1960: president, Dr. John R. Tobey, Newark; first vice-president, Dr. Eugene L. Miller, Newark; second vice-president, Dr. Samuel B. Kaplan, Elizabeth; treasurer, Dr. Morton Kulick, Paterson; recording secretary, Dr. Max Braitman, West New York; and corresponding secretary, Dr. Hugh McCulloch Jr., 68 Watchung Ave., North Plainfield, N. J.——The new officers elected at the annual meeting of the New Jersey Proctologic Society are as follows: president, Dr. Lloyd B. Whitman, Bergenfield; vice-president, Dr. Morando De Fronzo, Newark; secretary, Dr. Henry T. Weiner, Perth Amboy; and treasurer, Dr. Sydney S. Pearl, Elizabeth.

NEW YORK

Union Honors Rehabilitation Workers.—Dr. Michael M. Dacso, director of physical medicine and rehabilitation, specializing in rehabilitation of the aged at Goldwater Memorial Hospital, and Dr. Alvin I. Goldfarb, director of psychiatric and neurological services at the Home for Aged and Infirm Hebrews, were two of three persons who received the annual award of District 65, Retail, Wholesale and Dept. Store Union, AFL-CIO, for achievement in the field of welfare of the aged, May 27. Mr. G. Warfield Hobbs III, chairman, National Committee on the Aging, also was named. A fourth designee for an award, Senator Wayne Morse, appeared before a regular membership meeting of the 800 District 65 retirees June 1 to accept his citation. Dr. Dacso, who celebrates this year his 10th anniversary as director of the department of physical medicine and rehabilitation at Goldwater Memorial Hospital, was honored "for the promise he has helped to bring to thousands."

Society News.—At the annual meeting of the Rochester Academy of Medicine May 12 Dr. Conrad E. Good was elected to succeed Dr. Allan A. Fisher as president. Other officers elected for 1959-1960 are Dr. Theodore B. Steinhausen, vice-president; Dr. Robert E. Wells, secretary, and Dr. Stearns S. Bullen Jr., reelected treasurer.——The officers of the Queens Pediatric Society for the year 1959-1960 are as follows: president, Dr. Frederick Castrovinci, Jackson Heights; president-elect, Dr. Emanuel Fletcher, Flushing; secretary, Dr. Joseph Stein, Jamaica; and treasurer, Dr. Elmer E. Amerman, Jackson Heights.

New York City

Conference on Rehabilitation of Psychiatric Patients.—A work conference, "Rehabilitation of the Psychiatric Patient—An Interdisciplinary Approach to His Post-Hospital Adjustment," will be held at the Teachers College, Columbia University, and the Fountain House, New York City, July 6-24. The conference goal is to give students sufficient understanding of problems in rehabilitation of the mental patient during his post-hospital adjustment so that the students may develop and expand similar programs in their own communities. Participants will be required to devote their full day to the curriculum which will consist of morning lectures, discussions, and field visits, and afternoon participation in the program of the Fountain House, a psychiatric rehabilitation center. Coordinator of the program is Abraham Jacobs, Ph.D., professor of education, department of psychological foundations and services,, Columbia University. Fee for students enrolled for credit is $111 for tuition plus a $10 university fee. The conference is designed primarily for staff members of hospitals, rehabilitation centers, mental hygiene clinics, and similar facilities. Enrollment will be limited to 25 students. For information, write Dr. Abraham Jacobs, Box 35, Teachers College, Columbia University, New York 27.

NORTH DAKOTA

Dedicate Cancer Research Laboratory.—The Guy and Bertha Ireland Laboratory for cancer research was formally dedicated March 9-10 at the University of North Dakota, Grand Forks. Dr. James Frederic Danielli, British physiologist, was the main speaker. Dr. William E. Cornatzer, head of the biochemistry department at UND, presented a bound volume of reprints of the publications produced in the Ireland Laboratories. The Ireland Research Laboratory was established in 1953 with a bequest of $11,200 from the Irelands. Then, in 1957, Mrs. Bertha Ireland gave the department of biochemistry a grant of $75,000. The laboratory was constructed with the $75,000 from Mrs. Ireland, $74,190 from the National Institutes of Health, $50,000 from the North Dakota Medical Center, and $810 from research grants. The building is constructed so that in the future it may be expanded for three more floors to match the height of the Medical School Building. It has been designed as an open laboratory with 11 laboratories and two offices, five research laboratories, and a central laboratory bench with five chemical hoods. Other rooms include a glassware wash room, laboratory cold room for enzyme research, high-speed refrigerated centrifuge room, chromatography room, electrophoresis room, and geiger counter room. Twenty-four full- and part-time employees are engaged in biochemistry research at the university.

OHIO

Dr. Meade Gives Lecture.—The second George M. Curtis Lecture was given at the Ohio State University Health Center May 25 by Dr. Richard H. Meade Jr., of Grand Rapids, Mich., who presented "The Evolution of Pulmonary Resection." The George M. Curtis Lectureship was established in 1956 in honor of Dr. Curtis, professor emeritus of surgery at the Ohio State University Medical School, Columbus.

OREGON

Cancer Conference in Portland.—The first annual Oregon Cancer Conference, co-sponsored by the Oregon State Medical Society, the Oregon Division, American Cancer Society, and the University of Oregon Medical School will be held at the Library Auditorium of the University, July 16-17, in Portland. Two symposiums are planned: "Tumors of the Skin" and "Treatment of Cancer of the Endometrium." The following papers are scheduled:

The Present Position of Surgery in the Treatment of Cancer, Dr. John E. Dunphy, Boston.
Precancerous Dermatoses, Dr. Leslie M. Smith, El Paso, Texas.
Nevi, Juvenile Melanomas, Malignant Melanomas, and Experimental Melanomas with Differential Diagnostic Consideration, Dr. Arthur C. Allen, Miami, Fla.
Treatment of Skin Cancer, Dr. Smith.
Viruses and Cancer, Dr. Gilbert J. Dalldorf, New York City.
Diagnosis and Treatment of Cervix Cancer, Dr. Francis B. Carter, Durham, N. C.
Precision in Radium Therapy, Dr. Gilbert H. Fletcher, Houston, Texas.
Cancer Chemotherapy, Dr. Ralph Jones Jr., Miami, Fla.
Diagnosis and Treatment of Ovarian Cancer, Dr. Carter.
Supervoltage Therapy in Pelvic Cancer, Dr. Fletcher.

At the evening banquet, July 16, Governor Mark O. Hatfield, of Oregon, will speak. The program is accepted for category II credit by the American Academy of General Practice. For information, write Dr. Martin A. Howard, 1115 S. W. Taylor St., Portland 5, Ore., Chairman, Committee on Cancer.

PENNSYLVANIA

Art Collection at Hospital.—A collection of 50 paintings has been loaned to Montefiore Hospital, Pittsburgh, by Mr. and Mrs. Lawrence Rill Schumann, Boston art collectors. The Schumanns' collection is comprised of some 800 or 900 paintings from artists throughout the world. Numbering among them are works of such famous men as Renoir, Modigliani, Matisse, Vlaminck, and Genado. The paintings which are exhibited throughout the corridors, dining rooms, waiting rooms, and lobbies at Montefiore are of landscapes, flower designs, and still life. Mr. Schumann is the founder and president of the Lawrence Rill Schumann Art Foundation in Boston. The purpose of the foundation is to lend paintings and different subjects of art to hospitals and universities, throughout the country.

Philadelphia

Society News.—The following are the newly elected officers of the Philadelphia Allergy Society: president, Dr. Alexander M. Peters; vice-president, Dr. Charles H. Classen; and secretary-treasurer, Dr. Sonia Stupniker.——The annual business and scientific meeting of the Philadelphia Rheumatism Society was held on May 21. Election of officers followed the program: president, Dr. John Lansbury; vice-president, Dr. Joseph L. Hollander; and secretary-treasurer, Dr. William D. Kimler.——At the executive session of the Philadelphia Roentgen Ray Society May 7, the following officers were elected for the year 1959-1960: president, Dr. Herbert M. Stauffer; vice-president, Dr. J. Francis Mahoney; secretary, Dr. Robert B. Funch, department of radiology, Germantown Hospital, Philadelphia 44; treasurer, Dr. Randal A. Boyer; and councillor-at-large, Dr. John T. Brackin.

Dr. Mudd Becomes Professor Emeritus.—Dr. Stuart Mudd, chairman, Committee on Research, Council on Drugs, A. M. A., will relinquish his administrative duties in the department of microbiology, University of Pennsylvania School of Medicine, July 1, to become professor emeritus of microbiology. At the same time, he takes up an active professorship of microbiology (Henry Phipps Institute) in the department of public health and preventive medicine in the School of Medicine. He also becomes a project supervisor and consultant to the Veterans Hospital in Philadelphia, Sept. 1, and holds the office of president of the International Association of Microbiological Societies from 1958-1962. This is the microbiological division of UNESCO and comprises the national microbiological societies of 31 countries.

Personal.—Dr. I. S. Ravdin, vice-president for medical development and John Rhea Barton Professor of Surgery at the University of Pennsylvania, was appointed to serve a three-year term on the National Advisory Health Council.——Dr. Albert P. Seltzer was selected by the Veterans of Foreign Wars as the "Man of the Year" on May 20.——A testimonial dinner for Dr. Robert A. Kimbrough Jr., director, division of obstetrics and gynecology, Pennsylvania Hospital, since 1951, was held April 8. On hand were about 50 physicians who received their resident training under Dr. Kimbrough at either Pennsylvania or Graduate Hospitals, as well as a group of personal friends. A highlight of the evening's program was the presentation to Dr. Kimbrough of a plaque inscribed as follows: "An Affectionate Tribute to Robert Alexander Kimbrough, Jr., by his Residents in Appreciation of his Tireless Effort and Unfailing Loyalty as their Teacher, Counselor, and Friend."

Symposium Marks Opening of Laboratories.—A two-day symposium, "The Structure of Science," was held in Irving Auditorium at the University of Pennsylvania April 17 and 18 accompanying the formal opening of new laboratories and a new museum at the Wistar Institute of Anatomy and Biology in Philadelphia. Senator Lister Hill, of Alabama, and Dr. LeRoy Burney, surgeon general, U. S. Public Health Service, were among the speakers. Mayor Richardson Dilworth, of Philadelphia, welcomed program participants and guests and discussed Philadelphia as a center for basic research.

The reconstructed Wistar Institute of Anatomy and Biology.

The Wistar Institute, reportedly one of the nation's oldest privately endowed centers of basic biological research, was the scene of a reception and a tour of its new laboratories and museum April 18 following the afternoon session of the symposium's second day. The institute was founded in 1818 as the Wistar Museum. It housed the anatomical collection of Dr. Caspar Wistar, professor of anatomy and author of a text on this subject. The museum was expanded into a biological research institute in 1892 in consequence of gifts from Gen. Isaac J. Wistar, grandnephew of the founder. The Wistar Institute of Anatomy and Biology was formally opened in 1894 in a new building erected by Gen. Wistar and maintained by an endowment which he created. The original Wistar Institute building has been completely reconstructed during the past two years to provide new laboratories and a new museum. The institute is staffed with a team of international scientists interested in problems in cellular biology.

TEXAS

Personal.—Dr. James R. Schofield was promoted from assistant dean of the Baylor University College of Medicine to associate dean. The action was taken by the Houston Executive Committee of the Board of Trustees at its meeting on Jan. 20——The five-year appointment of Dr. Randolph Lee Clark Jr., Houston, as chairman, Committee on Cancer, American College of Surgeons, effective Sept. 27, was announced.

Dr. Schwarz Honored.—Dr. Edwin G. Schwarz, Fort Worth pediatrician, was honored April 7 at the eighth annual testimonial dinner given by the National Conference of Christians and Jews. Dr. Schwarz was cited for his "outstanding professional devotion to sick and crippled children of Fort Worth." Reportedly Fort Worth's first pediatrician, Dr. Schwarz organized the original Baby Hospital which became Fort Worth Children's Hospital. He is past-president of the Texas Pediatric Society.

WASHINGTON

Personal.—On Jan. 21 the appointment of Dr. Archibald L. Ruprecht as medical director of the Seattle pilot outpatient clinic for alcoholics was announced. The clinic is to be used as a study project in determining the effectiveness of outpatient psychiatric treatment of selected alcoholics.——Joan Jackson, Ph.D., research instructor, department of psychiatry, and Stanley Gartler, Ph.D., research assistant professor, departments of medicine and pediatrics, University of Washington School of Medicine, Seattle, have been named senior research fellows of the National Institutes of Health.

GENERAL

Society of Cybernetic Medicine Founded.—The International Society of Cybernetic Medicine was recently founded with the purpose of assembling researchers engaged in the study of cybernetics applied to medicine and biology, and diffusing the method of research based on analogic calculus, and the use of electronic models. Physicians, biologists, engineers, physicists, and mathematicians may become members of this society. Applications should be addressed to the Secretariat-General, presently located in Naples, Italy, 348 Via Roma. The society by-laws will be sent on request. Prof. Aldo Masturzo is president of the acting council.

Award for Essay on Goiter.—The American Goiter Association again offers the Van Meter Prize Award of $300 to the essayist submitting the best manuscript of original and unpublished work concerning "Goiter—especially its basic cause." The studies may relate to any aspect of the thyroid gland in all of its functions in health and disease. The award will be made at the fourth International Goiter Conference in London, England, July 5-9, 1960, where a place on the program will be reserved for the winning essayist if he can attend the meeting. For 1960, the recipient of the award will receive consideration for a travel honorarium. The essays may cover either clinical or research investigations, should not exceed 3,000 words in length, and must be presented in English. Duplicate typewritten copies, double spaced, should be sent to the Secretary, Dr. John C. McClintock, 149½ Washington Ave., Albany 10, N. Y., not later than Jan. 1, 1960.

Report on Decline of Hospital Construction.—New construction for philanthropic purposes—religious, educational, and hospital—totaled $484 million in the first quarter of 1959, according to the American Association of Fund Raising Counsel, Inc. Private hospital construction totaled $142 million, a decrease of 6% from last year. The capital needs of American hospitals were estimated by the association to require 501 million dollars annually for the next 20 years. Building in 1958 increased 20% over 1957, and totaled in excess of 600 million dollars, almost doubling 1956 expenditures. An estimated 275 million dollars a year will be required from private sources to continue needed capital development, according to the association. The American Association of Fund Raising Counsel is a nonprofit organization of 28 professional fund-raising firms engaged in organizing, counseling, and directing fund-raising activities in the United States and Canada. Its headquarters is 500 Fifth Ave., New York 36.

Report on Traffic Deaths.—A total of 10,690 persons died on the nation's highways in the first four months of this year, the National Safety Council reported. This was 4% more than the toll of 10,270 for the same period last year. Each of the four months brought more highway deaths than a year ago. The council estimates that highway accidents also brought disabling injuries to 400,000 persons in the four-month period. Despite the increase in traffic deaths, the mileage death rate for the first two months of the year (latest travel figures available) was the lowest on record for that period. This is because travel increased 6% while deaths went up 3%. This produced a mileage death rate (deaths per 100 million miles of travel) of 5.1, as compared with 5.2 for the same period last year. For the four-month period 19 states showed decreases while 30 had increases. Reports from 712 cities with more than 10,000 population showed they had an aggregate 5% decrease in April. For four months, these cities showed a 1% increase over last year.

Grants for Teaching and Research.—Unrestricted grants totaling $1,650,000 to 11 private medical schools in support of their teaching-research staff were announced by the Josiah Macy Jr. Foundation. The action was taken "in recognition of the fact that the adequate staffing of medical schools is the crucial problem of the national program of medical research and teaching." The foundation made grants of $50,000 per annum for a three-year period to each of the 11 private schools for strengthening their staff, particularly in the medical science departments. The schools are Yale University School of Medicine, New Haven, Conn.; University of Chicago, The School of Medicine; Johns Hopkins University School of Medicine, Baltimore; Harvard Medical School, Boston; Washington University School of Medicine, St. Louis; Columbia University College of Physicians and Surgeons, New York City; Cornell University Medical College, New York City; New York University College of Medicine, New York City; University of Rochester (N. Y.) School of Medicine and Dentistry; Vanderbilt University School of Medicine, Nashville, Tenn.; and Duke University School of Medicine, Durham, N. C.

Rocky Mountain Conference on Cancer.—The 13th annual Rocky Mountain Cancer Conference will be held July 22-23 at the Brown Palace Hotel, Denver. Dr. John I. Zarit, Denver, president, Colorado State Medical Society, will open the program with an address. Symposiums on cancer of the colon and anemia in cancer will be moderated by Drs. Kenneth C. Sawyer, and Matthew H. Block, respectively. The following papers are scheduled:

Chemotherapy of the Leukemias and Lymphomas, Dr. Edward H. Reinhard, Chicago.
Tumors of the Thymus Gland, Dr. Benjamin Castleman, Boston.
Cancer of the Prostate, Dr. Louis M. Orr, Orlando, Fla., President, A. M. A.
Carcinoma of the Stomach, Dr. Walter L. Palmer, Chicago.
Evaluation of Treatment of Carcinoma of the Breast in Its Total Pattern, Dr. J. Garrott Allen, Chicago.
Advances in Cancer Research and Control, Dr. James R. Heller, Bethesda, Md.
Some of the Intangibles Concerning Cancer, Dr. Eugene P. Pendergrass, Philadelphia.

For information write Mr. John W. Pompelli, Assistant Executive Secretary, Colorado State Medical Society, 835 Republic Bldg., Denver 2.

Project to Provide Building Accessibility.—At a conference held in Washington, D. C., 45 representatives of national groups recommended that the American Standards Association be asked to initiate a standards project that would make buildings used by the public and their facilities accessible to physically handicapped people. At the request of the President's Committee on Employment of the Physically Handicapped, the association called the conference to see if the national groups concerned could agree to try and help solve this problem. The meeting disclosed that specifications are needed for such things as stairs, doors, elevators, rest-room facilities, drinking fountains, and phone booths so that the handicapped will be able to use them. A draft guide aimed at overcoming some of these obstacles was prepared under the auspices of the President's Committee with the help of the Veterans Administration. The conference also recommended that the proposed national standards project be co-sponsored by the President's Committee and the National Society for Crippled Children and Adults, Inc. The American Standards Association is the national coordinating body for standardization in the United States. It is a federation of 122 trade associations and technical societies with more than 2,000 company members.

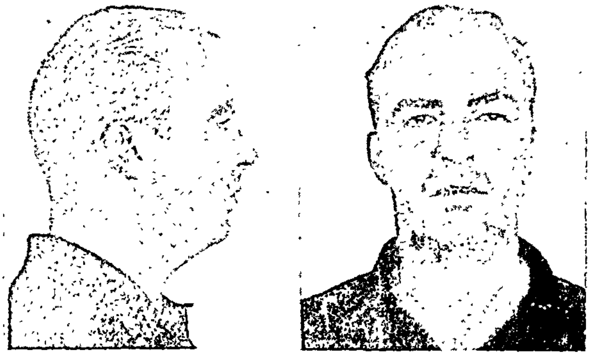
Rehabilitation Fellowship for Australian Physician.—The creation of the Frank H. Rowe Memorial Fellowship in Rehabilitation for postgraduate training in physical medicine and rehabilitation in the United States for a physician from Australia was announced recently. The fellowship is being given by the World Rehabilitation Fund, Inc., in cooperation with the Australian Advisory Council for the Physically Handicapped, the International Society for the Welfare of Cripples, and the Smith, Kline, and French Foundation. The fellowship was created to honor the late Frank H. Rowe, C. B. E., director-general of social services, Commonwealth of Australia, 1949-1958, "for his contribution to the development of rehabilitation services for the physically handicapped internationally." The fellowship is for a minimum of one year and is subject to renewal. Training will be given at the Institute of Physical Medicine and Rehabilitation, New York University-Bellevue Medical Center, New York City. Preliminary screening will be done by a selection committee appointed by the Australian Advisory Council for the Physically Handicapped. The World Rehabilitation Fund is a nonprofit organization supported by American industry, foundations, and individuals to assist in the international development of rehabilitation services for the physically handicapped.

Prevalence of Poliomyelitis.—According to the National Office of Vital Statistics, the following number of reported cases of poliomyelitis occurred in the United States, its territories and possessions in the weeks ended as indicated:

	May 30, 1959		May 31, 1958
Area	Paralytic Type	Total Cases	Total
New England States			
Maine	..	..	..
New Hampshire	..	..	..
Vermont	..	..	..
Massachusetts	..	..	..
Rhode Island	2	2	..
Connecticut	..	..	1
Middle Atlantic States			
New York	1	1	1
New Jersey	..	..	..
Pennsylvania	..	..	..
East North Central States			
Ohio	..	1	..
Indiana	2	2	..
Illinois	..	..	4
Michigan	..	3	..
Wisconsin	..	..	..
West North Central States			
Minnesota	..	..	..
Iowa	..	..	1
Missouri	..	..	..
North Dakota	..	..	..
South Dakota	..	..	..
Nebraska	1	1	..
Kansas	..	..	..
South Atlantic States			
Delaware	..	..	..
Maryland	..	..	..
District of Columbia	..	..	..
Virginia	1	2	1
West Virginia	1	2	..
North Carolina	..	..	1
South Carolina	..	..	..
Georgia	..	..	..
Florida	6	7	7
East South Central States			
Kentucky	2	2	..
Tennessee	2	2	1
Alabama	..	1	..
Mississippi	..	1	1
West South Central States			
Arkansas	..	..	..
Louisiana	3	3	..
Oklahoma	..	2	5
Texas	3	6	11
Mountain States			
Montana	..	1	..
Idaho	..	..	..
Wyoming	..	..	..
Colorado	..	..	..
New Mexico	1	1	..
Arizona	2	2	1
Utah	..	..	..
Nevada	..	..	..
Pacific States			
Washington	..	..	..
Oregon	1	1	..
California	5	5	6
Alaska	..	..	..
Hawaii	..	..	4
Puerto Rico	..	..	1
Total	33	48	46

Correspondence Course for Record Librarians.—Doris Gleason, C. R. L., executive director, American Association of Medical Record Librarians, announced a grant to the association of $88,540 from the W. K. Kellogg Foundation for establishing an extension-correspondence course for hospital employed medical record personnel. Named to direct the program is Sara McKinney, C. R. L., chief medical record librarian at the Hospital of the University of Pennsylvania, Philadelphia. This educational program will be available to all medical record personnel in the United States, and is designed to provide those who are handicapped by the lack of formal education in this specialty with basic training through an in-service educational program. Medical record science is taught in some 30 approved schools in the country, and a minority of medical record librarians reportedly have had the advantage of this formal education. The new extension-correspondence course is planned to embrace 25 lessons and one examination, to be completed in no less than 15 months and no more than 24 months. The course content will include orientation to the health, hospital, and medical record fields, medical terminology, coding of diseases and operations, and the various forms and methods for medical record keeping. For information, write the American Association of Medical Record Librarians, 840 N. Lake Shore Drive, Chicago 11.

Wanted by the FBI.—Clovis Odva Evans was sentenced in Federal Court in Miami, Fla., Nov. 26, 1954, to one year in prison for passing fraudulent checks. His sentence was suspended and he was put on probation for three years with the provision that he report to his probation officer monthly. He last reported on Sept. 6, 1955, when he told the probation officer that he had been arrested about three weeks earlier by the Miami Police Department and was charged with breaking and entering, grand larceny, and petty larceny, and that he was out on bond awaiting trial. He failed to appear for his trial, disappeared from his job and residence, and has not reported to his probation officer since. On Jan. 23, 1956, a Probation Violator's Warrant was issued for his arrest. Since childhood he has suffered from nephritis and heart disease. Evans, who has used several aliases, is usually known as "Bud," "Buddy," or "Scott." He is 35 years old, 6 ft. in height, weighs 200 lb., and has light brown hair and brown eyes. He has a ½ in. scar at outside corner of his left eye, a growth on the first joint of his right thumb; and a scar at the tip of his left index finger. He usually wears dark glasses in and out of doors. Any physician having information about this man should contact the nearest office of the Federal Bureau of Investigation.



Clovis Odva Evans.

Awards for Service to Disabled.—The International Society for the Welfare of Cripples and the Albert and Mary Lasker Foundation announced March 15 that three Albert Lasker awards for outstanding achievement in the development of services for the physically disabled will be presented at the society's eighth World Congress in New York City Aug. 30, 1960. The awards, made by the foundation through the International Society every third year, consist of $2,500 each, a citation and a silver statuette of the Winged Victory of Samothrace, symbolizing victory over death and disease. Their purpose is to emphasize, through the recognition of individual and group accomplishments which are internationally significant, the importance of developing improved services for the disabled persons of the world. An international committee will select the recipients from nominees proposed by affiliated national organizations of the society and other organizations carrying out programs for the disabled in various countries. The International Society for the Welfare of Cripples is a federation of voluntary organizations in 36 countries and is devoted to global cooperation in the development of services for the rehabilitation of handicapped men, women, and children. Dr. Howard A. Rusk, New York City, 1957 Albert Lasker award winner, is serving as president of the ISWC Eighth World Congress. The Albert and Mary Lasker Foundation established the Albert Lasker Awards in 1944 to honor and encourage outstanding achievement in medical research and public health administration.

Health Agency Donations.—Ten major national health agencies raised a total of $161,843,030 during the past fiscal year, The American Association of Fund Raising Counsel, Inc., reported May 13. All of the reporting agencies are known to the public for their annual national appeals. Individual expenditures in five major areas of service were reported by each agency where funds were expended. The following shows number of expenditures in each area:

Medical Treatment	39.5%
Community Service	20.5%
Lay & Medical Education	18.5%
Research Grants	12.5%
Fund Raising	12.5%
Other Purposes	10.5%

With the exception of one reporting agency showing 60.6% spent for medical treatments, the general disbursement of funds was relatively well balanced in each area. The association noted that the promotion of medical care and health services in the United States totals some 20.5 billion dollars a year, which is nearly 5% of the gross national product. The current national budget for the promotion of health provides 678 million dollars of which 40.7%, or 276 million dollars, will come from taxes.

The public is giving in excess of 162 million dollars for national health effort and 276 million dollars additional in tax money to promote public health, the association said. The American Association of Fund Raising Counsel, Inc. is a nonprofit organization of 28 professional firms engaged in counseling, directing, and organizing fund-raising activities in the United States and Canada.

Call for Gerontological Papers.—The Gerontological Society, Inc., announced that the 12th annual scientific meeting of the society will be held at the Statler Hotel, Detroit, Nov. 12-14, under the theme, "New Frontiers of Research and Training in Gerontology." Abstracts of papers should be submitted to the chairman of the appropriate section for consideration by the program committee. Abstracts of exhibits should be sent to the chairman of the exhibits committee. Chairmen of the five sections and exhibits committee are as follows:

Biological Sciences, Dr. Warren Andrew, department of anatomy, University of Indiana, School of Medicine, Indianapolis 7.
Clinical Medicine, Dr. Robert T. Monroe, Geriatric Clinic, Peter Bent Brigham Hospital, 270 Commonwealth Ave., Boston.
Psychological and Social Sciences, Marion E. Bunch, Ph.D., department of psychology, Washington University, St. Louis 5.
Social Welfare, Mr. Jerome Kaplan, Mansfield Memorial Homes, Inc., Walpark Building, Mansfield, Ohio.
General Membership, Mr. Herbert Shore, The Dallas Home for the Jewish Aged, 2525 Centerville Road, Dallas, Texas.
Exhibits Committee Chairman, Dr. Leo Gitman, Brooklyn Hebrew Home and Hospital for the Aged, Howard and Dumont Avenues, Brooklyn 12.

Deadline for sending abstracts is July 15. Abstracts should be submitted in duplicate, double-spaced, and include the title, authors, and institution or laboratory of origin. The text of abstracts should include the purpose of the investigation, general methods, material, and results or conclusions. The author should indicate if he will present lantern slides. Dr. A. Hazen Price, 62 W. Kirby Ave., Detroit, is chairman of the local arrangements committee, and Wilma T. Donahue, Ph.D., division of gerontology, University of Michigan, Ann Arbor, is the program chairman.

Society News.—The officers elected at the recent meeting of the **Society for Pediatric Research** are: president, Dr. Henry L. Barnett, New York City; vice-president, Dr. Frederic N. Silverman, Cincinnati; and for council, Drs. Edna H. Sobel, New York City, and Forrest H. Adams, Los Angeles. Dr. Clark D. West, Cincinnati, is secretary-treasurer.—At the annual meeting of the **American Goiter Association** May 1 the following officers were elected: president, Dr. Edwin G. Ramsdell, White Plains, N. Y.; president-elect, Dr. Alexander Albert, Rochester, Minn.; first vice-president, Dr. Howard R. Mahorner, New Orleans; second vice-president, Dr. William A. Meissner, Boston; third vice-president, Dr. Ray F. Farquharson, Toronto, Canada; secretary, Dr. John C. McClintock, Albany, N. Y.; treasurer, Dr. Theodore O. Winship, Washington, D. C.; and executive counselor, Dr. Lawrence W. Sloan, New York City (for four years). The 1960 meeting will be held jointly with the London Thyroid Club as the fourth International Goiter Conference in London, England, July 5-9, in the Royal College of Surgeons.—At the annual spring meeting of the **American Society of Facial Plastic Surgery** March 18 the following officers were elected: president, Dr. Oscar J. Becker, Chicago; vice-president, Dr. Sam H. Sanders, Memphis, Tenn.; treasurer, Dr. Joseph C. Miceli, Brooklyn; and secretary, Dr. Samuel M. Bloom, 123 E. 83rd St., New York 28. The meeting previously announced for July 15 will take place on July 17 in New York and will be for members only.—The officers of the **American Laryngological Association** for 1959-1960 are: president, Dr. William J. McNally, Montreal, Canada; secretary, Dr. Lyman G. Richards, Wellesley Hills, Mass.; treasurer, Dr. Francis E. LeJeune, New Orleans; and editor, historian, and librarian, Dr. Edwin N. Broyles, Baltimore. The 81st annual meeting will be held at the Deauville Hotel, Miami Beach, Fla., March 18-19, 1960.—At the recent **Harvey Cushing Society** meeting the following officers were elected for next year: president, Dr. James L. Poppen, Boston; vice-president, Dr. Francis Murphey, Memphis, Tenn.; president-elect, Dr. J. Granfton Love, Rochester, Minn.; historian, Dr. Louise C. Eisenhardt, New Haven, Conn.; secretary, Dr. Hendrik J. Svien, 200 First St., S. W., Rochester, Minn.; and treasurer, Dr. Eben Alexander Jr., Winston-Salem, N. C. Dr. Walter E. Stern, Los Angeles, was appointed chairman of the program committee for the next meeting which will be held in San Francisco.—The Holmes Lecture at the 40th annual meeting of the **New England Roentgen Ray Society** May 14 was delivered by Dr. Leo G. Rigler. His subject was "The Place of Radiology in Medical Education." The following officers were elected for the coming year: president, Dr. Stanley M. Wyman, Boston; president-elect, Dr. Arnold H. Janzen, Hartford, Conn.; vice-president, Dr. Donald P. Ham, Greenfield, Mass.; secretary, Dr. John E. Gary, Brookline, Mass.; treasurer, Dr. Lloyd E. Hawes, Boston; and executive committee member at large, Dr. Mirle A. Kellett, Boston.

FOREIGN

Congress on Physical Therapy in Paris.—The third International Congress of the World Confederation for Physical Therapy will be held in Paris, France, Sept. 6-12. The theme of the congress is "Physical

Therapy—Its Importance in Human Economic and Social Development" with emphasis on neurology, geriatrics, orthopedic surgery and traumatology, rheumatology, heart and chest conditions, aids and prostheses, and psychiatry. Information may be obtained from the American Physical Therapy Association, 1790 Broadway, New York 19.

Indian University Develops Biochemistry Department.—Teaching and research in biochemistry at the University of Lucknow, India, will be facilitated when new laboratories and classrooms are completed. To the funds for their construction provided by the University Grants Commission of India, the Rockefeller Foundation had added 201,700 rupees (about $42,800), available during the period ending March 31, 1962. A major center of higher education in northern India, the University of Lucknow has reportedly made a special effort within the past few years to develop training and research in biochemistry. Dr. P. S. Kirshnan has been appointed a professor at the university, and posts for two assistant professors of biochemistry have been created. The first group of graduate students is working under Dr. Kirshnan. With the funds provided by the University Grants Commission and the foundation, the university plans to construct a new teaching section, an adjacent research laboratory, and an animal house, as well as to augment its scientific equipment and library materials in the field.

CORRECTION

Vascular Accidents to the Brain Stem Associated with Neck Manipulation.—In the article by Green and Joynt in the May 30 issue, on page 522, line 7 of the second paragraph, the word pallesthesia should be allesthesia.

EXAMINATIONS AND LICENSURE

NATIONAL BOARD OF MEDICAL EXAMINERS

National Board of Medical Examiners: Various Centers: Part I only, Sept. 9-10. Examinations must be received at least six weeks in advance of a specific examination date. Examining centers established after close of registration. Exec. Sec., Dr. John P. Hubbard, 133 South 36th St., Philadelphia 4.

EDUCATIONAL COUNCIL FOR FOREIGN MEDICAL GRADUATES, INC.

Educational Council for Foreign Medical Graduates: Stations around the world, Sept. 22. Final date for filing applications is June 22. Succeeding examinations—March 16, 1960 and Sept. 21, 1960. Exec. Director, Dr. Dean F. Smiley, 1710 Orrington Ave., Evanston, Ill.

BOARDS OF MEDICAL EXAMINERS

Alaska:* On application in Anchorage or Fairbanks. Sec., Dr. W. M. Whitehead, 172 South Franklin St., Juneau.

Arizona:* *Reciprocity.* Phoenix, July 15-17. Exec. Sec., Mr. Robert Carpenter, 826 Security Bldg., Phoenix.

California: *Written.* Los Angeles, Aug. 17-20; Sacramento, October 19-22. *Oral.* Los Angeles, August 15; San Francisco, November 14. *Oral and Clinical.* Los Angeles, August 16; San Francisco, Nov. 15. Sec., Dr. Louis E. Jones, Room 536, 1020 N Street, Sacramento.

Colorado:* *Examination. Reciprocity.* Denver, July 14. Sec., Dr. John B. Farley, 712 Republic Bldg., Denver 2.

Connecticut:* *Examination.* Hartford, July 14-16. Sec., Dr. Staley B. Weld, 160 St. Ronan St., New Haven.

Delaware: *Examination.* Dover, July 14-16. *Endorsement.* Dover, July 23. Sec., Dr. Joseph S. McDaniel, Professional Bldg., Dover.

Guam: *Subject to Call.* Act. Sec., Dr. F. L. Conklin, Agana.

Hawaii: *Written.* Honolulu, July 13-14. Sec., Dr. I. L. Tilden, 1020 Kapiolani St., Honolulu.

Idaho: *Examination and Endorsement.* Boise, July 13. Exec. Sec., Mr. Armand L. Bird, 364 Sonna Bldg., Boise.

Illinois: *Examination.* Chicago, July 7-10. *Reciprocity.* Chicago, July 10. Supt. of Registration, Mr. Frederic B. Selcke, Capitol Building, Springfield.

Maine: *Examination and Reciprocity.* Augusta, July 14-16. Sec., Dr. Stephen A. Cobb, Sanford.

Montana: *Examination and Reciprocity.* Helena, Oct. 6. Sec., Dr. Thomas L. Hawkins, 555 Fuller Ave., Helena.

New Hampshire: *Examination and Reciprocity.* Concord, Sept. 9-12. Sec., Dr. Edward W. Colby, 107 State House, Concord.

North Carolina: *Endorsement.* Blowing Rock, July 24. Sec., Dr. Joseph J. Combs, Professional Bldg., Raleigh.

North Dakota: *Examination and Reciprocity.* Grand Forks, July 8-11. Sec., Dr. C. J. Glaspel, Box 228, Grafton.

Oregon:* *Examination.* Portland, July 7-9. *Reciprocity and Endorsement.* Portland, July 9-11. Exec. Sec., Mr. Howard I. Bobbitt, 609 Failing Bldg., Portland.

Pennsylvania: *Examination and Endorsement.* Philadelphia and Pittsburgh, July 1-3. Sec., Mrs. Margaret G. Steiner, Box 911 Harrisburg.

Puerto Rico: *Examination.* San Juan, Sept. 8. Sec., Dr. Joaquin Mercado Cruz, Box 9156, Santurce.

Rhode Island:* *Examination and Endorsement.* Providence, July 2-3. Administrator, Mr. Thomas B. Casey, 366 State Office Bldg., Providence.

South Dakota:* *Examination.* Sioux Falls, Aug. 25-26. Exec. Sec., Mr. John C. Foster, 300 First National Bank Bldg., Sioux Falls.

Utah: *Examination and Reciprocity.* Salt Lake City, July 8-10. Dir., Mr. Frank E. Lees, 324 State Capitol Bldg., Salt Lake City 1.

Washington:* *Examination.* Seattle, July 13-15. Administrator, Mr. Thomas A. Carter, Capitol Bldg., Olympia.

West Virginia: *Examination.* Charleston, July 13-15. *Reciprocity and Endorsement,* July 13. Sec., Dr. Newman H. Syer, State Office Bldg., No. 3, Charleston 5.

Wisconsin:* *Written.* Milwaukee, July 14-16. *Reciprocity.* Milwaukee, July 15. Sec., Dr. Thomas W. Tormey, Jr., 1140 State Office Bldg., Madison.

BOARDS OF EXAMINERS IN THE BASIC SCIENCES

Iowa: *Examination.* Des Moines, July 14. Sec., Dr. Elmer W. Hertel, Waverly.

Oklahoma: *Examination.* Oklahoma City, Sept. 25-26. Exec. Sec., Mrs. L. Haidek, 813 Braniff Bldg., Oklahoma City.

Tennessee: *Examination.* Memphis, June 30-July 1. Sec., Dr. O. W. Hyman, 62 South Dunlap St., Memphis 3.

Washington: *Examination.* Seattle, July 8-9. Sec., Mr. Thomas A. Carter, Capitol Bldg., Olympia.

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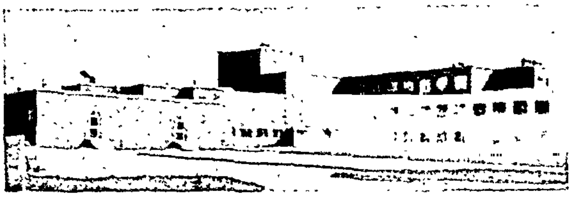
*Basic Science Certificate required.

GOVERNMENT SERVICES

AIR FORCE

International Air Show.—The Air Force School of Aviation Medicine participated in the 23rd International Air Show in Paris in June. The air show celebrated the 50th anniversary of the first international exposition, devoted solely to aeronautical science, and Bleriot's first flight across the English Channel. Col. Robert H. Blount, deputy commandant of the school, attended with a display of the physiological instruments evolved by the school for use in advanced scientific projects.

New U. S. A. F. Hospital.—The 100-bed United States Air Force Hospital at Forbes Air Force Base, Kansas, was opened in March. It will provide the following services: aviation medicine, general medicine, general surgery, obstetrics and gynecology, pediatrics, and radiology. Col. Jack F. Burnett, U. S. A. F., M. C., is commander of the hospital.



School of Aviation Medicine.—The Air Force School of Aviation Medicine will move from Randolph Air Force Base, near San Antonio, Texas, to new multimillion dollar quarters southwest of the city, in July. Of the seven buildings comprising the new institution, the Flight Medicine Laboratory, the Academic Building, and the Research Laboratory Shops are already occupied.

NAVY

Personal.—Capt. John W. Albrittain, Medical Corps, is now head of the Medical Corps Training Section, Training Branch, Bureau of Medicine and Surgery. Prior to his present assignment, he was on duty at the U.S. Naval Hospital, National Naval Medical Center, Bethesda, Md.

VETERANS ADMINISTRATION

Personal.—Dr. Thomas M. Arnett, Veterans Administration area medical director in Trenton, N. J., was appointed deputy director for planning in the VA Department of Medicine and Surgery in Washington, D. C., where he will assist Dr. Irvin J. Cohen, the VA assistant chief medical director for planning.

PUBLIC HEALTH SERVICE

New Pamphlet.—"The Report of the U. S. Public Health Mission to the Union of Soviet Socialist Republics" (PHS publication 649) may be purchased from the Superintendent of Documents, U. S. Government Printing Office, Washington 25, D. C., at 45 cents a copy. This report contains the findings of a mission of five doctors who visited the Soviet Union in 1957. They traveled 8,500 miles and visited 61 institutions in nine cities in five of the Soviet Republics. They found that the problem of medical care in the Soviet Union has been tackled with great vigor. There is a high ratio of physicians to total population, but the Soviet government has deliberately focused on quantity and widespread coverage of personnel and services at the expense of quality. There are, however, certain ingredients in their political system which permit astonishingly rapid change-over and developments in medicine as impressive as the appearance of the first man-made earth satellite. Pestilential diseases and the diseases of filth have been substantially brought under control. Malaria as a significant health problem is on the way to eradication. Venereal disease has been mastered, but tuberculosis remains a plague.

The five-man mission consisted of Dr. Thomas Parran, Chairman, former Surgeon General of the U. S. Public Health Service; Dr. Otis L. Anderson, Assistant Surgeon General for Personnel and Training, Public Health Service; Dr. Henry van Zile Hyde, Assistant to the Surgeon General for International Health, Public Health Service; Dr. Malcolm Merrill, California State Director of Public Health; and Dr. Leonid S. Snegireff, Associate Professor of Cancer Control, Harvard School of Public Health.

Preventing Hot Weather Diseases.—Suggestions for avoiding the diseases and accidents that take their heaviest toll in hot weather such as poliomyelitis, diarrhea, heat stroke and prostration, sunburn, swimming hazards, water-borne diseases, tetanus, poison ivy, plant allergies, rabies, snake bites, and insect hazards are given in a series of health leaflets prepared by the Public Health Service. Single copies may be obtained by writing the Public Health Service, Washington 25, D. C.

Dr. Ravdin on Health Council.—Dr. Isidor S. Ravdin, Vice-president for Medical Development at the University of Pennsylvania, was appointed to serve a three-year term on the National Advisory Health Council in which capacity he will advise and make recommendations to the surgeon general of the Public Health Service on matters relating to health activities and functions of the service. He will also advise on the activities of the Division of General Medical Sciences of the National Institutes of Health.

DEATHS

Bartels, Richard Rauch Ⓜ Albuquerque, N. M.; Chicago Medical School, 1930; member of the American Trudeau Society; from 1943 to 1947 medical director of the New Mexico State Tuberculosis Sanatorium in Socorro; died in the Presbyterian Hospital April 3, aged 60.

Beagle, John S. Ⓜ Sidney, Mont.; the Hahnemann Medical College and Hospital, Chicago, 1896; died April 2, aged 85.

Bivings, Charles Knox Ⓜ Albuquerque, N. M.; University and Bellevue Hospital Medical College, New York City, 1923; interned at the Bellevue Hospital in New York City; fellow of the American College of Surgeons; veteran of World War I; associated with Presbyterian Sanatorium and St. Joseph Sanatorium and Hospital; died in Mexico April 3, aged 60.

Blachly, Lucile Spire Ⓜ Oklahoma City, Okla.; Rush Medical College, Chicago, 1916; member of the American Rheumatism Association; served as director of child hygiene for the state health department; died April 2, aged 76.

Carnes, Edwin Hammond Ⓜ Hartford, Conn.; born in Thomastown, Miss., June 22, 1897; University of Tennessee College of Medicine, Memphis, 1921; fellow of the American College of Surgeons; member of the Aero Medical Association; pursued an extensive and varied career in the U. S. Public Health Service from which he retired March 1, 1956; formerly senior medical officer at the U. S. Coast Guard Academy in New London; received the Army Commendation Ribbon for his contribution to the Alaska Military Highway project in 1943; served as director of the U. S. Marine Hospital in New Orleans; for many years chief medical officer in charge of the U. S. Marine Hospital in Memphis, Tenn.; at one time first vice-president of the Memphis Symphony Society; chief of the division of hospitals of the state department of health; died in St. Francis Hospital April 13, aged 61.

Cregar, Peter Bodine, Plainfield, N. J.; University of Pennsylvania Department of Medicine, Philadelphia, 1899; for many years associated with the Muhlenberg Hospital, where he died April 8, aged 88.

Danforth, Theodore Loring, Buffalo; Johns Hopkins University School of Medicine, Baltimore, 1936; interned at Buffalo General Hospital in Buffalo and the Franklin Square Hospital in Baltimore; served a residency in psychiatry at Sheppard and Enoch Pratt Hospital in Towson, Md., and Butler Hospital in Providence, R. I.; died in Stamford Hall in Stamford, Conn., Jan. 3, aged 49.

Davis, Clara M. Ⓜ Winnetka, Ill.; University of Michigan Department of Medicine and Surgery, Ann Arbor, 1904; member of the American Academy of Pediatrics; served with the Red Cross overseas during World War I; formerly associated with the Children's Memorial Hospital in Chicago; died April 8, aged 80.

Delany, George Joseph, New York City; Columbia University College of Physicians and Surgeons, New York City, 1936; specialist certified by the American Board of Surgery; fellow of the American College of Surgeons; veteran of World War II; on the staff of St. Vincent's Hospital and secretary of its alumni association; died April 6, aged 48.

Derrington, Albert Emry Ⓜ Kansas City, Mo.; University of Kansas School of Medicine, Kansas City, Kan., 1945; interned at the Naval Hospital in Portsmouth, Va.; served in the Naval Reserve from July 2, 1945 to Dec. 29, 1946; on the medical staffs of Providence Hospital in Kansas City, Kan., Research, and St. Mary's hospitals; died March 14, aged 37, aboard an ocean liner bound for Italy.

Fike, Ralph Llewellyn Ⓜ Wilson, N. C.; born in Union, S. C., March 14, 1905; Medical College of South Carolina, Charleston, 1932; member of the American Academy of General Practice; past-president of the Wilson County Medical Society and the Fourth District Medical Society; served as chairman of the board of education; the new senior high school in Wilson was named in his honor last year; the Wilson unit of the North Carolina Education Association named him "Layman of the Year in Education" in 1956; past-president of the North Carolina School Boards Association; a director of the North Carolina Tuberculosis Association; for many years associated with the Woodward-Herring Hospital, where he died March 30, aged 54.

Fish, Ezra Simpson Ⓜ Camarillo, Calif.; born in Meadville, Pa., in 1886; University of Pennsylvania School of Medicine, Philadelphia, 1912; specialist certified by the American Board of Pediatrics; member of the American Academy of Pediatrics; emeritus professor of pediatrics at the University of Southern California School of Medicine in Los Angeles; during World War I served as a captain in the Cabot Medical Unit with the British Forces;

Ⓜ Indicates Member of the American Medical Association.

bacteriologist for the Rhode Island State Board of Health from 1914 to 1916; on the staff of the Childrens Hospital and the Hospital of the Good Samaritan in Los Angeles, where he died April 5, aged 72.

Floersch, Michael A. Ⓜ Topeka, Kan.; John A. Creighton Medical College, Omaha, 1900; on the staff of St. Francis Hospital; died March 31, aged 83.

Gillespie, S. Crawford Ⓜ Asheville, N. C.; University of Cincinnati College of Medicine, 1932; veteran of World War II; staff member of Memorial Mission, St. Joseph's and Aston Park hospitals; died April 2, aged 58.

Grothaus, John B. Ⓜ Hamilton, Ohio; Medical College of Ohio, Cincinnati, 1894; died in the Mercy Hospital March 9, aged 91.

Jaffe, Nathan Bernard, New York City; University of Vermont College of Medicine, Burlington, 1917; fellow of the American College of Gastroenterology; member of the American Trudeau Society and the Association of Military Surgeons of the United States; died in St. Vincent's Hospital March 22, aged 69.

Jarzab, Walter Anthony Ⓜ Niagara Falls, N. Y.; Hahnemann Medical College and Hospital of Philadelphia, 1934; associated with Mount St. Mary's and Memorial hospitals; died March 16, aged 49.

Kempf, Arthur Reginald Ⓜ Springfield, Tenn.; University of Tennessee College of Medicine, Memphis, 1905; past-president of the Robertson County Medical Association; veteran of World War I; on the staff of the Jesse Holman Jones Hospital; past-president of the Springfield Lions Club; died in the Jesse Holman Jones Hospital March 3, aged 75.

Kistler, Chester K. Ⓜ Reading, Pa.; Jefferson Medical College of Philadelphia, 1897; past-president of the Berks County Medical Society; veteran of World War I; emeritus consultant in medicine at St. Joseph's Hospital; died March 27, aged 85.

Kitchen, Philip Gordon Ⓜ Pocono Lake, Pa.; University of Pennsylvania School of Medicine, Philadelphia, 1911; member of the American Academy of General Practice; died in the General Hospital of Monroe County, East Stroudsburg, March 28, aged 73.

Koscianski, Leo Casimer Ⓜ Rochester, N. Y.; University of Buffalo School of Medicine, 1924; member of the American Academy of General Practice; veteran of World War I; a staff member of the St. Mary's Hospital, where he died March 24, aged 59.

La Camera, Frank Ⓜ Warren, Ohio; University of Cincinnati College of Medicine, 1921; member of the American Academy of General Practice; on the staffs of the Trumbull Memorial and St. Joseph's Riverside hospitals; died in the Southside Unit of the Youngstown Hospital, March 22, aged 65.

Leach, William Otto Ⓜ La Crescenta, Calif.; Wisconsin College of Physicians and Surgeons, Milwaukee, 1908; veteran of World War I; member of the Association of Military Surgeons of the United States; affiliated with Glendale Sanitarium and Hospital and the Memorial Hospital of Glendale; died in the Mission Sanitarium in Glendale March 8, aged 82.

Lee, J. Marshall Ⓜ Newton Grove, N. C.; Medical College of Virginia, Richmond, 1916; served as a member of the North Carolina General Assembly; died March 15, aged 73.

Liburt, Joseph Ⓜ Huntington, N. Y.; Detroit College of Medicine and Surgery, 1925; specialist certified by the American Board of Proctology; veteran of World War I; associated with South Side Hospital in Bay Shore, Central Islip (N. Y.) State Hospital, and the Huntington (N. Y.) Hospital, where he died March 26, aged 60.

Livingston, Fred Johnson Ⓜ Macedonia, Ohio; University of Toronto Faculty of Medicine, Toronto, Ont., Canada, 1913; member of the American Psychiatric Association; served with the Royal Medical Corps and the Royal Canadian Medical Corps in World War I; in 1937 joined the staff of Hawthornden State Hospital; died in Huron Road Hospital in East Cleveland March 19, aged 68.

Lobsenz, Moses Ⓜ New York City; University and Bellevue Hospital Medical College, New York City, 1911; specialist certified by the American Board of Obstetrics and Gynecology; fellow of the American College of Surgeons; veteran of World War I; for many years on the staff of the Beth David Hospital; died in Lenox Hill Hospital March 29, aged 72.

Luckemeyer, Carl Joseph, St. Cloud, Minn.; Marquette University School of Medicine, Milwaukee, 1943; member of the American Academy of General Practice; from 1953 to 1955 in the military service; president-elect of the staff of St. Cloud Hospital, where he died March 13, aged 41.

MacKnight, William Frank Ⓜ Fall River, Mass.; Harvard Medical School, Boston, 1913; veteran of World War I; served as chairman of the board of health and the board of trustees of the Fall River General Hospital; died in St. Anne's Hospital March 20, aged 71.

McCann, Florence Edith Ⓜ Milwaukee; University of Illinois College of Medicine, Chicago, 1914; served on the staffs of Milwaukee and Columbia hospitals; until 1954 medical director of the Planned Parenthood Clinic, of which she was founder; a founder of the Milwaukee Goodwill Industries; died in the Milwaukee County Hospital, Wauwatosa, March 19, aged 72.

McGuire, M. Ruth Ⓜ Detroit; University of Illinois College of Medicine, Chicago, 1916; affiliated with Woman's Hospital; medical director of the Merrell Palmer School; died in the Woman's Hospital March 22, aged 65.

O'Crowley, Clarence Rutherford Ⓜ Christmas Cove, Maine; born in Newark, N. J., May 8, 1880; Columbia University College of Physicians and Surgeons, New York City, 1904; veteran of the Spanish-American War and World War I; specialist certified by the American Board of Urology; member and past-president of the American Urological Association and the American Association of Genito-Urinary Surgeons; fellow of the American College of Surgeons; past-president of the New York Urological Society, Essex County (N. J.) Medical Society, Essex County (N. J.) Pathological and Anatomical Society, and the Society of Surgeons of New Jersey; in 1947 received the Edward J. Ill Award from the Academy of Medicine of Northern New Jersey; formerly instructor in urology at the New York Post-Graduate Medical School and Hospital in New York City, and assistant professor of urology at the Medico-Chirurgical College, Graduate School of Medicine, University of Pennsylvania, Philadelphia; formerly practiced in Newark, N. J., where he was associated with the Newark City Hospital, Newark Beth Israel Hospital, and Presbyterian Hospital; consultant in urology at many hospitals in New Jersey; served on the staff of St. Mary's Hospital in Orange; on the staff of the Miles Memorial Hospital in Damariscotta; served on the advisory board of *The Urologic and Cutaneous Review* and the *American Journal of Surgery;* died March 28, aged 78.

Okel, James LeRoy, Lieut., M. C., U. S. Navy, Montgomery, Ala.; Medical College of Alabama, Birmingham, 1957; interned at Naval Hospital in Oakland, Calif.; appointed an ensign in the U. S. Naval Reserve in April, 1955, and commissioned a lieutenant in the U. S. Navy in June, 1957; reported for active duty on June 26, 1957; a student flight surgeon, attached to the School of Aviation Medicine at the Naval Air Station in Pensacola, Fla.; died March 4, aged 26.

Pilling, George Platte Jr. Ⓜ Philadelphia; Jefferson Medical College of Philadelphia, 1903; member of the American Urological Association; died Feb. 23, aged 86.

Pretlow, William Ribble Ⓜ Warrenton, Va.; Medical College of Virginia, Richmond, 1934; interned at the Medical College of Virginia Hospital Division in Richmond; member of the American Academy of General Practice; on the staff of the Fauquier Hospital; died March 29, aged 49.

Ray, Richard Horace Ⓜ Corpus Christi, Texas; St. Louis University School of Medicine, 1936; veteran of World War II; on the staffs of Spohn, Memorial and Driscoll Foundation hospitals; died in Phoenix, Ariz., April 2, aged 47.

Rivenburgh, Willard T. Ⓜ Middleburg, N. Y.; University of Buffalo School of Medicine, 1886; past-president of the Schoharie County Medical Society; served as president of the board of education; at one time held a position as school inspector with the New York State Health Department at Albany; for many years coroner of Schoharie County; served as health officer of the village and town of Middleburg and the towns of Fulton, Blenheim, and Gilboa; died in the Ellis Hospital, Schenectady, March 24, aged 95.

Rosen, William Ⓜ New Bedford, Mass.; Medical School of Maine, Portland, 1912; since 1935 medical examiner for the Bristol South District; associated with St. Luke's Hospital; died March 27, aged 69.

Ryan, Thomas Joseph Ⓜ Philadelphia; born in Gilberton, Pa., Dec. 4, 1896; University of Pennsylvania School of Medicine, Philadelphia, 1919; specialist certified by the American Board of Surgery; certified by the National Board of Medical Examiners; fellow of the American College of Surgeons; member of the Philadelphia Academy of Surgery; past-president of the Delaware County Medical Society; a member of the board of directors of the Associated Hospital Service of Philadelphia; member of the lay board of directors of Villanova University; a member of the board of directors of the Medical Club of Delaware County; director of surgery at Fitzgerald Mercy Hospital in Darby, Pa.; since 1920 a member of the staff and since 1953 medical director of the Misericordia Hospital, where he was a member of the lay advisory board, and where he died April 2, aged 63.

Salley, E. McQueen Ⓜ Hendersonville, N. C.; University of Maryland School of Medicine, Baltimore, 1905; for many years physician for the Southern Railway; died March 15, aged 78.

Scott, Hamil Smyth, Kingsport, Tenn.; Medical College of Virginia, Richmond, 1906; veteran of World War I; died in the Veterans Administration Hospital, Roanoke, Va., March 14, aged 79.

Snead, Calvin Bee Harris, Columbia, Tenn.; Meharry Medical College, Nashville, Tenn., 1916; died March 7, aged 76.

Sosman, Merrill Clary Ⓜ Boston; born in Chillicothe, Ohio, June 23, 1890; Johns Hopkins University School of Medicine, Baltimore, 1917; specialist certified by the American Board of Radiology; professor emeritus of radiology at Harvard Medical School, where he joined the faculty in 1922 as an instructor in roentgenology, subsequently serving as assistant professor, clinical professor, clinical professor of radiology, and professor of radiology; vice-chairman, Section on Radiology of the American Medical Association, 1938-1939, and chairman, 1939-1940; member and past-president of the Harvey Cushing Society and the American Roentgen Ray Society; in 1947 Caldwell lecturer; past-president of the New England Roentgen Ray Society; in 1947 George W. Holmes lecturer; member of the Radiological Society of North America and in 1957 received its gold medal; member of the American College of Radiology, American Academy of Arts Sciences, and Sigma Xi; fellow of the American Association for the Advancement of Science; served in the regular Army; veteran of World War I; consultant in radiology at the Massachusetts General Hospital; chairman emeritus of the radiology department at the Peter Bent Brigham Hospital, where a portrait of him was unveiled in 1947 by his colleagues; served on the staffs of the Children's Hospital, and Boston Psychopathic Hospital in Boston, and Cape Cod Hospital in Hyannis; died in the Peter Bent Brigham Hospital March 28, aged 68.

Stein, Aron Ⓜ Philadelphia; Medizinische Fakultät der Universität, Wien, Austria, 1930; member of the American Academy of General Practice; associated with Frankford Hospital and the Albert Einstein Medical Center; died Feb. 23, aged 62.

Stephenson, Albert Otto Ⓜ Chicago; Chicago Medical School, 1926; veteran of World War I; for many years on the staff of the Jackson Park Hospital; died March 28, aged 65.

Tanner, Evans Martindale Ⓜ Bluefield, W. Va.; Medical College of Virginia, Richmond, 1908; long time member of the medical staff of Bluefield Sanitarium; died in Staunton, Va., March 30, aged 80.

Thomason, Eddie Houston Ⓜ Olanta, S. C.; Medical College of South Carolina, Charleston, 1931; charter member of the American Academy of General Practice; past-president of the Florence County Medical Society; veteran of World War II; for 12 years a trustee of the Olanta High School; died in the Johns Hopkins Hospital, Baltimore, March 28, aged 50.

Trapold, Augustine Charles Ⓜ Akron, Ohio; University of Pennsylvania School of Medicine, Philadelphia, 1919; formerly practiced in Wilkes–Barre, Pa., where he was city school director and on the staff of the Mercy Hospital; during World War II served in Norway with an American Scandinavian Field Hospital unit; died March 19, aged 62.

Turner, William Reson Ⓜ Fort Dodge, Iowa; Drake University College of Medicine, Des Moines, 1908; died in the Mercy Hospital March 25, aged 74.

Vaughn, Esther A. Brown, Louisville, Ky.; Louisville National Medical College, Medical Department State University, Louisville, Ky., 1905; died March 19, aged 78.

Vetkoskey, Caroline Ⓜ Havertown, Pa.; Woman's Medical College of Pennsylvania, Philadelphia, 1922; certified by the National Board of Medical Examiners; associated with the Delaware County Hospital in Drexel Hill, Pa., and the Woman's Hospital in Philadelphia; died April 3, aged 62.

Ward, Harley E. Ⓜ Pemberville, Ohio; Physio-Medical College of Indiana, Indianapolis, 1902; for many years surgeon for the New York Central Railroad; for 16 years a member of the school board; died March 20, aged 84.

Warnell, John Braxton Ⓜ Cairo, Ga.; Atlanta College of Physicians and Surgeons, 1900; served on the state board of medical examiners; formerly mayor and member of the city council; died March 12, aged 81.

Watson, Samuel Park, New Bern, N. C.; University of Maryland School of Medicine, 1901; at one time associated with the New York City Board of Health; died March 16, aged 86.

Weiswasser, E. Frank Ⓜ Rego Park, N. Y.; L. R. C. P., of Edinburgh, L. R. C. S., Edinburgh, and L. R. F. P., & S., of Glasgow, Scotland, 1947; interned at the Lebanon Hospital in New York City; served on the staffs of the Jamaica and Queens General hospitals in Jamaica; died in the Forest Hills (N. Y.) General Hospital, March 9, aged 45.

Westbrooks, Orlando L., Nashville, Tenn.; Meharry Medical College, Nashville, 1932; died in the George W. Hubbard Hospital of Meharry Medical College March 20, aged 58.

Whalen, Joseph Francis Ⓜ Evanston, Wyo.; University of Nebraska College of Medicine, Omaha, 1927; veteran of World War II; past-president of the Uinta County Medical Association; member of the American Psychiatric Association; superintendent and medical director of the Wyoming State Hospital; died March 21, aged 55.

Woodhouse, George Raymond Ⓜ Vinton, Iowa; State University of Iowa College of Medicine, Iowa City, 1908; for many years secretary-treasurer of the Benton County Medical Association, of which he was past-president; served as secretary of the park board, of which he was a member for 30 years; affiliated with Virginia Gay Hospital; president of the Vinton Building and Loan Association; died in St. Luke's Hospital in Cedar Rapids, March 18, aged 75.

Woodland, Charles Theodosius Ⓜ Baltimore; Howard University College of Medicine, Washington, D. C., 1929; vice-president of the staff of the Provident Hospital; died March 25, aged 55.

FOREIGN LETTERS

AUSTRIA

Treatment of Subdural Hematoma.—At the meeting of the Society of Physicians in Vienna on April 3, Dr. A. Gund of Bad Ischl stated that the mortality rate from chronic subdural hematoma is still exceedingly high (about 20%) despite the simplicity of the operation for its relief. This may be the result of postoperative complications, particularly hypotension. Since intraspinal injections of isotonic sodium chloride solution in the course of the operation have been used to prevent hypotension, the death rate among the speaker's patients has been greatly reduced. It is not known whether the favorable effect was due to a change in the pressure conditions or to the rapid formation of adhesions between the hematoma surfaces.

Autonomic Nervous System.—At the same meeting Dr. G. Lassmann stated that an attempt was made to find a relationship between clinical observations and a tendency to hyperplasia of the peripheral autonomic nervous system. The capacity for hyperplasia is in a similar way inherent in the ganglion cells and in the protoplasmic end-formations. It occurs in the ganglionic regulation centers in the form of compensatory hypertrophy which occasionally leads to the destruction of the cellular elements, and it has been described in patients with peripheral circulatory disturbances. Similar behavior has also been observed in a patient with bilateral sympathectomy for hypertensive disease.

The hyperplasia of the end-formations which leads to the formation of neuromas is of great clinical significance because it is associated with symptoms which may already be recognized. The appendix is an ideal test organ for this new growth, whose causes and extent are not yet known. The formation of a neuroma in this organ, which can be confirmed easily because this organ is easily visible, may represent a process which is limited locally and is, therefore, surgically curable, or it may represent the local acme of a multilocular growth. In the latter case the presence of a neuroma, which has been confirmed by operation, will induce the physician to consider and to analyze the continued symptoms from a different point of view. It is hoped that a meaningful consideration of the findings in the peripheral autonomic nervous system in combination with anatomicopathological and clinical considerations may lead to a desirable widening of our knowledge.

BRAZIL

Institute of Tropical Medicine.—The Institute of Tropical Medicine of São Paulo, a part of the School of Medicine of the University of São Paulo, was opened in January. This new institute has a department of microbiology and immunology under the direction of Dr. C. S. Lacaz, a department of parasitology headed by Dr. A. D. F. Amaral, and wards for tropical and infectious diseases under the direction of Dr. J. A. Meira. The Institute's administrative board is composed of the director of the faculty, Prof. J. A. Pupo, and the three abovementioned professors. A modern rickettsial and viral laboratory building, also part of the institute, is almost finished.

CANADA

Mental Depression.—In March the department of psychiatry of McGill University, Montreal, organized an international conference on mental depression. Lehmann of Montreal pointed out the lack of experimental data on depression and the impossibility of making the diagnosis on objective grounds. He believed that the differential diagnosis of endogenous or reactive depression should be made, however difficult. Sargant of London, England, agreed that a classification of depression was necessary, if only to prevent therapeutic mistakes, and suggested that the response to treatment might be a help to classification. Cleghorn of Montreal proposed the terms "manifest and latent depressive affect" for patients with and without somatic symptoms associated with depression. Noting the wide variety of somatic complaints which might either accompany or mask depression, he observed that no diagnostic help could be obtained from laboratory studies.

Lunn of Copenhagen favored the concept of depressive equivalents, and thought it hard to distinguish between psychological and somatic complaints; for example, fatigue might be physical or mental. Hoch of New York doubted that different psychodynamic mechanisms could be demonstrated in different types of depression; depression could scarcely be predicted from a study of a premorbid personality. The role of psychotherapy in association with electroshock or drug therapy has not been proved, and psychotherapy, as the sole treatment in endogenous depression, does not give impressive results. The preventive role of psychotherapy is also doubtful. Roth of Durham, England, found it dif-

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The items in these letters are contributed by regular correspondents in the various foreign countries.

ficult to distinguish at times between anxiety neurosis and depression, but believed that the distinction was necessary because of the unfortunate consequences of electroshock in the former condition.

The question of treatment of depression centered mainly around electroshock and imipramine. Hoff of Vienna thought that electroshock still gave the best results in endogenous depression (success in 80%) but had also treated patients with imipramine by parenteral injection or by mouth. Imipramine produced euphoria in depressed but not in normal persons. Hoff started with administration of 150 to 250 mg. of imipramine by injection daily, switching to oral doses of 300 mg. a day, and then tapering down to a maintenance dose. He usually gave the drug for 8 to 14 days, and if an effect was not obtained he used electroshock. Results were better in milder cases of endogenous depression. He warned of the risk of suicide if outpatients were not carefully observed by their psychiatrists while under drug treatment. Sargant pointed out that many patients with depression were given electroshock on an outpatient basis in Britain without unfavorable consequences.

Sigg of New York described his studies with imipramine, which in animals did not increase psychomotor activity and induced sedation when given in large doses. It did not antagonize the sedative effect of reserpine, and it preserved temperature regulation. It diminished susceptibility to electroshock and showed anticholinergic properties besides enhancing the vasopressor response of levarterenol. It was not an inhibitor of amine oxidase. Freyhan, of the University of Pennsylvania, gave 75 to 450 mg. of imipramine a day in three divided doses for 30 to 60 days. In patients with manic-depressive psychosis optimal results were obtained in 51% and partial modification of symptoms in 27%. Women responded better than men and younger patients better than older.

Deniker of Paris gave the drug to 137 patients with all types of depression with a 40% rate of success. A stable result was usually obtained in two to four weeks, the best results being in those with simple depression. Very few patients with depression resisted both imipramine and electroshock therapy. Himwich, of the University of Illinois, described his studies of the effects of imipramine on rabbits in which small doses inhibited the electroencephalographic signs of arousal on pain stimulus, acting synergistically with chlorpromazine but antagonizing reserpine. Imipramine increased the serotonin content of the brain and also the catecholamine content. Shepherd of London pointed out that properly conducted clinical trials of electroshock therapy had never been made, and he doubted whether it influenced the natural course of a depression. Sloane of Kingston, Ont., also expressed doubts about the value of electroshock in modifying the natural history of depression. Kielholz of Basel, Switzerland, had used imipramine for two years and found that it improved 60% of patients in 3 to 21 days. He found combination of the drug with electroshock therapy helpful. Ayd of Baltimore had similar results. He kept his dosage down to 200 mg. a day, and if necessary added 10 to 20 mg. of methylphenidate twice a day to abolish dizziness and faintness. His rate of failure was 27%. He mentioned the appearance of cardiac symptoms in some patients but believed that imipramine was in general a safe drug.

Cameron of Montreal stated that psychotherapy was required for neurotic depression, therapy with imipramine for simple mild or moderate endogenous depression, electroshock therapy for more severe depression with agitation, and preventive electroshock at intervals for recurrent endogenous depression. He had also found imipramine of value in treating elderly persons suffering from frustration and decrease in enthusiasm. Kalinowsky of New York had found a basic difference in action between electroshock, which he still believed was the preferred treatment, and imipramine therapy. He had found iproniazid helpful in patients in whom shock therapy had failed. Sargant had also used small daily doses of iproniazid to prevent recurrence of depression, with only one case of jaundice so far. Schneider of Lausanne, Switzerland, did not think that there was any fundamental difference in action between electroshock and imipramine. He used the drug extensively in place of shock and obtained results in patients in whom the latter had proved ineffective.

Lehmann summed up the relative values of electroshock and imipramine therapy, pointing out that electroshock was more predictable and would help any depression, being indicated when the risk of suicide was high. The statement that electroshock might shorten treatment is doubtful, and the fact that it is cheaper should not be a determining factor. Fink, of Glen Oaks, N. Y., noted that the behavioral and electroencephalographic changes with imipramine were most like those with central anticholinergic agents. Several speakers mentioned the side-effects of imipramine, which included dryness of the mouth and excessive sweating in over 50% of patients, gastrointestinal disturbances, dizziness, palpitation, tremor, disturbances of vision, allergic rash, and anuria.

Low Back Pain.—A series of 1,291 patients with low back pain coming before the Ontario Workmen's Compensation Board was reviewed by McCracken (*Canad. M. A. J.* 80:331, 1959), who showed that degenerative disease of the spine occurs much earlier in life than has been suspected. It is the greatest factor in producing herniated nucleus pulposus. Operation for this condition should be reserved for patients with multiple episodes of disability or continued severe disability. The true acute disk derangement with progressive paralysis was rare in this series. It is not the man's occupation that wears out his back, but the back which wears out the worker. He estimates that a workmen's compensation board may expect to assume 100% liability in compression fractures of spine, 75% liability in contusions and low back strain, 50% liability in herniated nucleus pulposus, and 25% liability in spondylolisthesis and spondylolysis.

In this series age had no appreciable influence on the occurrence of accidents, but it affected recuperative power. Few fractures of the spine or derangements of disks were produced by accidents. Of patients with back pain 75% had a simple low back strain which responded to conservative treatment in one to four weeks. There were twice as many patients with permanent disability after fracture of the spine than after low back strain or nonoperative disk herniations. Operative disk herniations carried the highest rate of permanent disability of all types.

Blood Cholesterol Levels.—Two recent publications in the *Canadian Journal of Biochemistry and Physiology* (37:479, 575, 1959) dealt with serum cholesterol levels. Rona and co-workers made some unexpected findings in rabbits fed an unsaturated fatty acid preparation containing 90 to 95% of linoleic acid. Atherosclerosis was produced in the rabbits by feeding them cholesterol by stomach tube, and the effects of the unsaturated fatty acid on cholesterol levels and production of atherosclerosis were studied. Not only did the free unsaturated fatty acids fail to prevent development of hypercholesteremia and atherosclerosis but they also had a deleterious action in comparison with a control series receiving olive oil.

Beveridge and co-workers gave a group of university students a fat-free homogeneous liquid formula ration for eight days. They then transferred groups to diets in which 30% of the calories were supplied in the form of butter or oil fractions substituted for carbohydrate. The most volatile fraction, which was rich in cholesterol, caused a sharp rise in plasma cholesterol levels, whereas fractions poor in cholesterol led to relatively small increases. Supplementing the cholesterol-poor fraction with amounts of cholesterol equivalent to those provided by the cholesterol-rich fraction raised the plasma level comparably. Their studies suggested that dietary cholesterol content can affect plasma cholesterol levels in a highly significant manner in man, and that the response obtained depends on the nature of the fat with which the sterol is associated.

Hodgkin's Disease.—Warwick and Sellers (*Canad. M. A. J.* 80:423, 1959) reviewed a series of 960 patients with Hodgkin's disease. About 80 deaths a year occur from this disease in Ontario (population 5,500,000), and the death rate from Hodgkin's disease is just over 1% of all cancer deaths. About 10% had had symptoms for over two years before reporting for treatment. Nearly 80% were treated by radiotherapy alone, the rest by combinations of chemotherapy, surgery, and radiotherapy. The crude five-year survival rate for all 960 cases was 29.7%, and it is noted that Hodgkin's disease is not invariably rapidly fatal, for eight persons survived for 10 years, six for 20 years, and four for at least 25 years.

Poliomyelitis.—The only area in Canada with a poliomyelitis epidemic in 1958 was the city of Winnipeg, Manitoba, where 76 cases were reported. The highest incidence of the disease was in the age group under 4 years, 82% of cases in this group being paralytic. Only 2 of the 52 paralyzed patients had received three doses of vaccine, and one of these had not received the third dose at the recommended interval of seven months. Hence a high degree of protection against type 1 virus was obtained with use of the recommended vaccine program. Use of gamma globulin in household contacts appeared to be of definite value. It was suggested by Cadham and Davies (*Canad. M. A. J.* 80:436, 1959) that those who had resided in Winnipeg since the epidemic in 1953 had a relatively high degree of naturally acquired immunity.

Spontaneous and Habitual Abortion.—A further report on the interdisciplinary study of spontaneous and habitual abortion at Dalhousie University appeared in the *Canadian Psychiatric Journal* (4:1, 1959). The team involved included an obstetrician, an endocrinologist, a psychiatrist, a biochemist, a pathologist, and a psychologist. The object of the study was to investigate the determinants suggested as having causative significance in premature interruption of pregnancy. The experimental group consisted of 100 patients who were thoroughly investigated from the obstetric point of view by chemical studies of the blood and urine, psychiatric interviews, psychological testing, and examination of the aborted fetus and placenta.

It was demonstrated that the levels of vitamin C and E in the blood were not significantly different in women who abort spontaneously than in normal pregnant women, that organic changes in the genital tract were relatively absent, and that the endocrinologic findings were somewhat complicated, the prognosis in pregnancy being on the whole poorer in patients with low hormonal levels. Psychiatric study uncovered two principal groups of women who abort spontaneously: (1) an "inadequate reserve" group, consisting of 44 women who appeared to have inadequate psychological and physical reserves to cope with the demands of normal pregnancy; and (2) an "independent-frustrated" group, also of 44 women, with higher intellectual levels and social adjustment.

A more intense study of 17 women who aborted habitually whose progress was followed week by week through pregnancy suggested that the urinary level of chorionic gonadotropin fell coincidentally with emotional upsets, that the estrogen and/or pregnanediol levels also tended to fall under emotional stress, and that levels of 17-ketosteroid excretion fluctuated within wide ranges. The pathologist demonstrated changes in the placentas of women who aborted spontaneously similar to those found in collagen diseases. In association with these findings it was shown that the serum of women who threatened to abort contained a large amount of sheep red cell–agglutinating substances in fluctuating titer. Studies in these 17 patients have developed into a therapeutic program, including psychiatric interviews weekly throughout pregnancy. As a result 15 of these women carried through to the birth of 17 children.

GERMANY

Treatment of Pancreatitis.—Kallikrein and trypsin are present in an inactive form in the healthy pancreas. In pancreatic disease the inactive trypsinogen is converted into the active, protein-splitting trypsin. The trypsin which is activated in the gland, instead of in the intestinal juice, effects further conversion of trypsinogen into the proteolytic enzyme by autocatalysis. The fact that trypsin also converts the inactive precursor kallikreinogen into the hypotensive kallikrein in the pancreas may explain the occurrence of autodigestive processes of the pancreas and severe symptoms of hypotension in pancreatic disease. Sufficient amounts of inactivator are present in the body under normal conditions, but these quantities do not apparently suffice to inactivate the pathologically increased amounts of enzyme formed in the presence of pancreatic changes. Kallikrein inactivator is then administered to mitigate the effects of the pathologically elevated trypsin and kallikrein levels in blood and tissues.

E. Werle and co-workers (*München. med. Wchnschr.* 100:1265-1267, 1958) gave kallikrein inactivator to 16 patients with acute pancreatitis and pancreatic necrosis. In many cases improvement was noted after only a few intravenous injections of the substance. The often unbearable pain was relieved after only a few hours. The markedly reduced blood pressure increased rapidly, often reaching normal values within several days. The greatly increased diastase values, amounting to several hundred Wohlgemuth units, usually returned to normal within a few days. These results were confirmed by R. Bedacht (*Ärztl. Praxis* 12:371-376, 1958) in a series of 10 similar cases. Latent irritation of the pancreas, often associated with diseases of the gallbladder or stomach, increased the likelihood that an operation would be necessary. Kallikrein inactivator should therefore also be given preoperatively and postoperatively when abdominal operations are performed, if the pancreas is believed to be involved.

Latex Fixation Test and Erythrocytic Agglutination.—W. Müller and E. Schupp (*Ztschr. Rheum.* 18:97, 1959) reported comparative studies with the latex fixation test of Singer and Plotz and the erythrocytic agglutination reaction of Waaler and Rose in 257 patients with rheumatic diseases, 50 patients with nonrheumatic diseases, and 30 healthy controls. Both tests generally gave concordant results. Discordant results of both reactions were caused by false-positive and more rarely false-negative results of the hemagglutination reaction rather than by a false result of the latex fixation test. In rare cases abnormalities of the rheumatoid arthritis factor itself caused the discrepancy. Neutralization of the rheumatoid factor with alpha globulin produced a nearly parallel fall of titer with the hemagglutination and the latex fixation test.

Of the rheumatic diseases typical progressive rheumatoid arthritis most often gave positive results with both tests. On the other hand, chronic polyarthritides with a cyclic course rarely gave positive results. In ankylosing spondylitis, menopausal and psoriatic arthropathies, and degenerative joint diseases both tests were always negative. In nonrheumatic diseases positive reactions were seldom seen. The latex fixation test is preferred to the hemagglutination test for the demonstration of the rheumatoid factor because it is more reliable and the test material is more easily obtained and preserved than that used for the hemagglutination test.

Another series of 256 patients (including 77 with rheumatoid arthritis) was examined by latex fixation test, hemagglutination reaction with sensitized sheep erythrocytes, L-agglutination, O-agglutination, and antistreptolysin reaction by F. Harter (*Ztschr. Rheum.* 18:150, 1959). He also found the latex fixation test to be superior to the others for the diagnosis of rheumatoid arthritis.

NORWAY

Influenza in School Children.—The outbreak of Asian influenza in the fall of 1957 enabled M. M. Hovland (*Tidsskrift for den norske laegeforening*, March 1, 1959) to study the behavior of the disease in the population of Bergen. The reactions of school children to it were measured by absences from school for sickness from week to week. The curve indicating these absences rose at an explosive rate, reaching its maximum of 16.2% in the middle of October. There was a fairly rapid fall thereafter and by the second week in November it had come down to the normal level of about 6%. The reactions of the adults to the epidemic was measured by sickness payments to wage-earners under the national health insurance scheme. The curve indicating these payments rose somewhat more slowly from the beginning of October, and it did not reach its maximum until the first week in November. Thereafter it showed a rapid fall, and by the end of the month it had reached the normal for that time of the year. The fact that the curve for school children reached its maximum a fortnight earlier than the curve for adults was interpreted by the author as showing that school children contract influenza at school rather than at home. A corollary to this conclusion is that if children could be kept away from schools, cinemas, and other meeting places, the spread of influenza could be delayed, if not prevented.

Iproniazid for Depressions.—At the women's department of the Dikemark mental hospital J. O. Haug and co-workers (*Tidsskrift for den norske laegeforening*, March 1, 1959) used iproniazid, beginning with 50 mg. thrice daily by mouth for a week and a supplement of 1 mg. of reserpine in the evening, on a series of 15 patients. As soon as a definite effect was achieved the dosage was reduced to 50 or 100 mg. daily and the reserpine was discontinued. All medication was usually discontinued when a remission had been effected. A complete or partial remission was recorded in 12 of the 15 patients, including 5 with definite melancholia, all of whom showed a complete remission. The partial improvement observed in one patient was followed by rapid transition to severe mania. None of the patients with senile depression showed any improvement. A moderate fall of the blood pressure occurred in about 50% of these and troublesome giddiness in about 33%. This necessitated the discontinuation of the drug in only one patient. Constipation, disturbed sleep, and stranguria were common side-effects. Only after the drug had been given for one to four weeks did the side-effects and the therapeutic effects appear.

Botulism from Trout.—Hitherto the cases of botulism recorded in Norway have been traced to hams, pickled pork, and home-canned meat cakes. Now salted trout has been incriminated by O. Bjerke and co-workers (*Tidsskrift for den norske laegeforening*, March 1, 1959). A previously healthy man aged 34 suffered from dryness of his mouth and throat, lack of visual accommodation, slight anisocoria, and nystagmoid movements on glancing to either side. These symptoms appeared after the patient had eaten a large quantity of fresh-water trout, lightly salted after being gutted, sliced open, and exposed to air for some time. It had then been packed in slabs in a barrel, with a weak salt solution on top to prevent air reaching it. Samples of the patient's blood and of the suspected fish were sent to a laboratory. Small quantities of botulinus toxin, type B, were found in the blood and a moderate amount of the same toxin was found in the trout. Probably the toxin had already reached the gut of the fish before it was slashed open, but the flesh of the fish may also have been contaminated while it lay on soil awaiting salting and further preparation. Four other men who ate trout from the same barrel were not affected, but they had not eaten such great quantities.

Thioridazine in Psychiatry.—At the Dikemark mental hospital comparative tests with chlorpromazine and thioridazine were made on 44 women by J. O. Haug (*Tidsskrift for den norske laegeforening*, March 15, 1959). Nearly all of these patients suffered from chronic schizophrenia of many years' standing, and their ages ranged from 30 to 62 years. They had all been treated more or less satisfactorily with chlorpromazine in doses of 100 to 500 mg. daily. The chlorpromazine was discontinued for a week or two before the patients were given the thioridazine, the dosage of which was 100 to 350 mg. daily for four weeks alternating with placebo tablets for four weeks. The results clearly favored thioridazine compared with the placebo or the chlorpromazine. The absence of drowsiness was noticeable when thioridazine was used, the patients becoming more awake and energetic than when chlorpromazine was given. Not one of the 44 refused the drug or asked for a return to chlorpromazine therapy, although this drug had a more rapid and probably also more antipsychotic effect than thioridazine. Thioridazine was well tolerated and caused no serious side-effects.

Interstitial Fibrosis of the Lungs.—K. A. Larsen (*Acta path. et microbiol. scandinav.* 45:167-185, 1959) described five cases of diffuse progressive interstitial fibrosis of the lungs in four men and one woman, all at least 63 years of age. Most of these cases were of relatively long duration. The main symptoms were progressive dyspnea, cough, and, later, cyanosis. In some there was clubbing of the fingers and "watch-glass" nails, and in the later stages there were signs of failure of the right ventricle. Radiologically there were progressively increasing numbers of small opacities in both lungs, some miliary and some forming a network. In other areas the opacities were more diffuse, with small cystic translucencies often close together. Pathological study showed the lungs to be firm and sometimes rubbery, with microscopic disappearance of respiratory epithelium and compact fibrosis with marked development of reticulin fibrils. Small cystic spaces lined with epithelium similar to that in bronchioles were also formed.

The author's observations pointed to a respiratory viral infection as the primary process. In three patients there was an introductory acute febrile respiratory infection which was suspected of being viral pneumonia, and in one patient such an infection led to death in five weeks. The respiratory symptoms and radiologic opacities had, in most patients, progressively increased after the acute respiratory infection. It was considered highly probable that the primary process was a viral infection affecting the bronchioles and more distal air spaces, followed by relatively extensive epithelial necrosis and sometimes also necrosis of the interstitial mesenchymal tissue in the same areas. Such extensive necrosis might lead to collapse of the reticular framework in the alveolar walls, making orderly regeneration of the pulmonary lobules with the respiratory elements impossible. Cystic spaces form between the collapsed areas and these become lined with epithelium from the remaining bronchioles or small bronchi. Proliferation of the mesenchymal tissue and formation of numerous reticulin fibrils occurs. Thus a pulmonary cirrhosis develops in much the same way as viral hepatitis produces cirrhosis of the liver.

Aneurysms as Complications of Angiography.—K. Liverud (*J. Oslo City Hosp.* 8:11-12, 209-219, 1958) reported a series of about 700 cerebral angiographies performed by the normal percutaneous technique with three deaths. In these three cases an obliterating dissecting aneurysm was formed on injection of the contrast medium at the site of puncture of the common carotid artery. Death was attributed to obliteration of the carotid artery. The angiographies were performed by three physicians, which makes it unlikely that the deaths were due to an individual error in technique. The accidents were caused by the sharp tip of the needle in the vessel wall during injection. In order to prevent further accidents of this kind the author considered it essential to alter the technique and to replace the sharp needle in the vessel by a flexible polyethylene catheter introduced percutaneously.

Care of Alcoholics.—In September, 1951, the Oslo branch of Alcoholics Anonymous opened its hospital, the A Clinic, which now has 37 beds and a staff of five physicians. One of them, T. G. Carlsen (*Tidsskrift for den norske laegeforening,* March 15, 1959) reported a series of 3,006 patients, all men, treated at the hospital from its opening to the end of 1957. While 2,530 of them had been admitted only once, the rest had been admitted two or more times. All admissions were voluntary, but many of them reflected the pressure put on the patients by the force of circumstances. Most of the admissions were the outcome of the good services of some member of Alcoholics Anonymous. All the diagnoses of patients at discharge were the work of the senior physician, who found chronic alcoholism or incipient chronic alcoholism in 86%; the remaining 14% could be classified as abusus ethylicus, dipsomania vera, or "admitted for observation." The 2,598 patients included in the 86% conformed to the same alcoholic pattern whatever their age, psychic equipment, environment, or provocative factors. The author believed the diagnosis of chronic alcoholism must depend on conformity to this pattern. In 1,478 patients (49%) primary psychic abnormalities were demonstrable. Carlsen concluded that these patients should learn to regard their condition as a disease whose component elements must be understood if it is to be combatted successfully.

Cerebral Atrophy.—L. Eitinger (*Nord. med.* 61:301-303 [Feb. 19] 1959) pointed out that cerebral atrophy has become an increasingly frequent finding in mental patients. He stated that pneumoencephalography in a series of 238 patients supported the opinion that in some persons cerebral atrophy may occur without progressive dementia. It was presumed that these patients had atrophy of the brain without any direct causal relationship to the particular psychiatric findings. The possibility that atrophic changes may have developed in early childhood must be considered. This might alter the person's reaction pattern, increase his vulnerability, and lower his resistance to psychic trauma. Therefore, patients with cerebral atrophy should also be subjected to rigorous psychotherapy, and the results need not necessarily be poorer than those in corresponding psychiatric patients without cerebral atrophy.

Myelography.—A series of 427 myelographies performed with use of a water-soluble contrast medium (methiodal) was reported by P. Kolstad and G. H. Solem (*Nord. med.* 61:306-309 [Feb. 19] 1959). In 173 cases laminectomy was performed. A correct diagnosis was made in 155 or 89.5% of these; 13 patients or 7.6% with uncertain or negative myelographic findings were found to have disk prolapse situated extremely laterally in the vertebral canal and not affecting the dural sac in 10 of these. Some of these patients also had short root sheaths, making a myelographic diagnosis impossible. In five cases or 2.9% with positive myelograms the pathological findings were described as arachnoiditis, vascular malformations, and cicatrices after earlier laminectomy. No serious complication was observed. A slight fall in blood pressure was offset by administration of ephedrine and oxygen. Pain in the lumbar region radiating to the lower extremities required use of a spinal anesthetic in three patients.

SWEDEN

Intellectual Work and Life Expectancy.—Intellectual work and study do not give rise to causes of death differing from those affecting persons in other kinds of work, according to Professor E. Ask-Upmark of Uppsala, Sweden. His investigation covered 382 university scholars (mostly professors), a group of 700 American professors, 741 streetcar conductors, and 508 typographers who died in 1957. The author found that the Swedish professors had an average life span of 68 years as compared with 61 years for the streetcar conductors and 58 years for the typographers. For the American professors the average life span was 67 years, 67% of the latter reaching 65 years, while only 33% of the Swedish streetcar conductors and typographers attained that age. Contrary to what had previously been believed in some quarters the intellectual strain to which professors were exposed did not increase the risk of brain tumors or cerebral hemorrhage. Of the 382 investigated 151 had died from cardiovascular diseases, 53 from cerebrovascular diseases, 53 from malignant tumors, and 34 from diseases in the respiratory organs. Cases of tuberculosis, pulmonary cancer, and suicide were few among the professors.

Fatty Acid, Glyceride, and Phospholipid Levels After Operation.—L. B. Wadström (*Acta chir. scandinav.* 116:167-180, 1958-1959) reported on the postoperative concentrations in plasma of unesterified fatty acids (UFA), glycerides, and phospholipids in 12 patients. Of these cholecystectomy was performed on seven, aged between 19 and 39 years, and herniorrhaphy on five, aged between 18 and 35. On the first postoperative day the same type of change in plasma lipid composition was found in both groups: an increased level of UFA and a decreased concentration of glycerides and phospholipids. Patients undergoing cholecystectomy were subjected before the operation to a restricted caloric regimen consisting solely of carbohydrates, identical to that used after operation. In this way the examinations were duplicated and the patients served as their own controls. The changes in plasma lipid composition during the two periods were on the whole the same. This indicated that the postoperative changes in plasma lipid concentrations might be the product of the restricted caloric regimen, but a significant difference was noted between the values recorded on the first postoperative as compared with those of the first preoperative day. There was an increase in UFA and a decrease in glycerides.

When semistarvation was combined with surgical trauma a more pronounced increase in the level of the plasma UFA was observed. The author found it difficult to decide whether the increased UFA level was due to an increased flow of UFA into or a delayed flow of UFA from the plasma. There were, however, indications that the increased level of UFA observed on the first postoperative day was an expression of an increased inflow from fat depots. A surgical trauma gives rise to an increased liberation of epinephrine, and epinephrine added to adipose tissue in vitro liberates UFA. The observation that UFA is extracted from plasma by cardiac and working skeletal muscles, together with the rapid output of carbon dioxide after intravenous injection of radioactively labeled UFA, indicates the importance of UFA in plasma as a transport form of fat for metabolic demands. The author believed that the glyceride level in plasma was probably related to the metabolic state of the body and dependent on the carbohydrates available for combustion.

Hyperparathyroidism and Peptic Ulcer.—J. Hellström (*Acta chir. scandinav.* 116:207-221, 1958/1959) analyzed a series of 121 patients with hyperparathyroidism. In this series the incidence of peptic ulcer was 28.6% in men and 4.6% in women. The age at which ulcer symptoms first appeared varied between 20 and 51 (average 37) years. In most patients the ulcer symptoms started long before hyperparathyroidism was diagnosed. A study in the whole population showed the incidence of peptic ulcer to be greatly raised in patients with hyperparathyroidism. In the patients with coincident hyperparathyroidism and peptic ulcer reported in the literature a remarkable feature was the presence in many patients of multiple adenomas or primary hyperplasia of the parathyroids, as well as of pathological changes in other endocrine organs. The author concluded that in some patients with these two conditions the relation was coincidental and in others there was some relation between them, probably chiefly in the form of an unfavorable influence on healing of the ulcer. In some patients other endocrine factors, particularly in the form of so-called ulcerogenic tumors of the pancreas, affected the development of peptic ulcers complicating hyperparathyroidism.

Clearance of Radiosodium from the Tendo Calcaneus.—The clearance rate of radioactive sodium (Na^{24}) injected locally in the tendo calcaneus was studied in a series of 60 men by K. Håstad and coworkers (*Acta chir. scandinav.* 116:251-255, 1958/1959). The series was divided into four groups, group 1 consisting of 12 persons with a mean age of 23; group 2 of 19 persons with a mean age of 43; group 3 of 16 persons with a mean age of 71; and group 4 of 13 persons with a rupture of the tendo calcaneus on the side not examined and a mean age of 43 years. The rate of absorption was significantly greater in group 1 than in groups 2 and 3 and it was also probably significantly greater in group 1 than in group 4. No significant difference was found between groups 2 and 4. The study therefore showed the rate of absorption in the tendon to decrease fairly steeply during the early phase of adult life, owing probably to a reduction in blood flow. On the other hand, no significant difference was found between a group of patients with rupture of the tendon and a control group with a similar age distribution, although such a difference might have been expected due to the probable degenerative cause of ruptures of the tendo calcaneus.

Peptic Ulcer due to Corticosteroids.—P. O. Gedda and U. Moritz (*Acta rheumatol. scandinav.* 4:249-256, 1959) compared the autopsy material from 31 patients who had rheumatoid arthritis not treated with corticosteroids with clinical material from 69 patients who were given 5 to 15 mg. of prednisone or prednisolone daily for at least six months. The frequency of peptic ulcer in the autopsy material was about 10% and in the clinical material it was 19%. Half the patients treated with corticosteroids had gastric complaints. The symptoms of the verified ulcers were often mild or atypical. None of the patients who were free from gastric complaints during the treatment had any provable ulcers. Such complications as perforation or hemorrhage may appear suddenly. The risk of ulceration increases with the duration of the steroid therapy.

Joint Symptoms and Panniculitis.—During a short period 13 patients with simultaneously appearing joint symptoms and dermal changes, the latter often primarily regarded as erythema nodosum, were observed by C.-M. Fajers and S. Thune (*Acta rheumatol. scandinav.* 4:286-295, 1959). The dermal epithelium was essentially normal and in most patients the cutis presented no changes. In two patients, however, a slight edema was observed as well as single sparse perivascular round cell infiltrations in the deepest part of the cutis. Only at the border between the cutis and the subcutaneous fatty tissue and particularly within the latter were there marked histological changes, which in all the patients presented manifestly homogeneous findings and the character of panniculitis. The apparently accidental association of joint symptoms and panniculitis may not be unusual since joints and fatty tissue are both of mesenchymal origin. In rheumatic diseases there is a general attack on the mesenchyme. It would seem, however, that this combination is not etiologically homogeneous. It is probably seen in typical rheumatic diseases, on the one hand, but it may also be an expression of a more nonspecific allergy in the fatty tissue and joints, on the other. From the point of view of clinical course and differential diagnosis, the observation is valuable. From the pathogenetic point of view it shows that the fatty tissue is often involved in mesenchymal processes, which must be regarded as allergic whether the allergy is caused by an earlier or simultaneous infection, tissue decomposition, or drugs.

Polyneuritis due to Nitrofurantoin.—Nitrofurantoin in a daily dosage of 300 to 500 mg. for 10 days or more caused polyneuritis in five patients, as reported by T. Hafström (*Opuscula med.* 4:17-23, 1959). Three of the patients showed signs of renal insufficiency. The prognosis was fairly good in four patients as most of the weakness disappeared and the paresthesias decreased. After 12 to 18 months some symptoms still remained. In the presence of renal insufficiency the author recommended that the daily dose not exceed 200 mg. and that it be given for not more than five days.

Familial Splenic Anemia.—In the pediatric clinic at Boden a study was made of 12 children with familial splenic anemia by P. O. Hillborg (*Nord. med.* 61:303-306 [Feb. 19] 1959). The first symptoms appeared at an early age, in 10 patients before 1 year and in 2 before 6 months. Of the latter two patients one exhibited several neurological manifestations and had a typical case of the rapidly progressive infantile form of the disease. Splenectomy was performed on eight patients and was indicated because of either a heavy spleen causing mechanical obstruction or panhematopenia. The four children who were not operated on died before the age of 3 years. Two of those operated on also died. Preoperative thrombocytopenia, leukopenia, and anemia were present. Postoperatively the thrombocyte counts were normal and the leukocyte counts high, but the anemia was not affected. A preoperative tendency to hemorrhage remained in two patients despite normalized thrombocyte counts. This might indicate that the tendency to hemorrhage in familial splenic anemia depends on some factor other than thrombocytopenia, possibly deposition of Gaucher's cells in the walls of the small vessels, with accompanying fragility of the vessels.

All the six patients on whom splenectomy was performed who were alive in July, 1958, had advanced skeletal changes. These consisted of bone necrosis in the hips resembling that seen in Perthes' osteochondrosis, kyphosis, and areas of decalcification in the long bones. In many patients the skeletal changes appeared shortly after splenectomy. The high incidence and early onset of these changes might suggest that splenectomy would hasten the deposition of lipids in the skeletal system. This result should be expected if kerasin, the lipid deposited in familial splenic anemia, were transported in the blood to be ingested by the phagocytes of the reticuloendothelial cells in different organs. Attempts to demonstrate kerasin in serum by several workers gave negative results.

Micromastia.—A. Ragnell (*Nord. med.* 61:350-354 [Feb. 26] 1959), in discussing micromastia, distinguished among different types, such as pure atrophy with ptosis, aplasia or hypoplasia of the breasts, mutilations after amputation of part of the breasts, and inhibition of growth after radiotherapy or excessive scarring of the skin. Because of the psychic suffering caused by the breast deformity and the uncertain and merely temporary effect of hormonal therapy in these patients, who generally are endocrinologically normal, plastic surgery is indicated. In patients with pure atrophy the author used a modification of the derma-fat transplantation, introduced by Berson and Bames, and contralateral transplantation of a resected piece of glandular tissue in unilateral micromastia with hypertrophy of the other breast. In a series of 22 patients who were operated on subjectively and objectively satisfactory results were noted in 67%, despite absorption of about 33% of the transplanted tissue. Lactation during pregnancy was reduced, but generally it did not fail completely.

Levarterenol for Barbiturate Poisoning.—G. von Reis (*Opuscula med.* 4:50-52, 1959) treated 870 patients in whom barbiturate intoxication had caused a fall in the blood pressure with intravenous infusion of levarterenol. A dose of 4 to 12 mg. per day was usually sufficient but doses up to 115 mg. were sometimes needed. The amount of fluid given intravenously, however, did not exceed 2,500 ml. per day. In these patients no anuria occurred, which was considered to be due to the maintenance of a satisfactory level of the blood pressure.

UNITED KINGDOM

Athletes Light Smokers.—Top athletes do not smoke much. This finding by a medical research team which questioned Empire Games competitors is published in *Physical Recreation*, the journal of the Central Council of Physical Recreation. No swimmers of either sex smoked. Among 285 competitors 16% smoked to some degree; 7% smoked fewer than 5 cigarettes a day; about 5% between 6 and 10; and just over 4% more than 11 a day. There was one light smoker among the cyclists. Two of the women athletes smoked a little. The heavier smokers were the boxers, fencers, weight-lifters, and male athletes competing in field events. Of 136 athletes interviewed 13 smoked between 1 and 5 cigarettes a day, 10 between 6 and 10, and 6 smoked 11 or more. Three of 19 boxers smoked 11 or more cigarettes a day, as did 3 of 12 weight-lifters. Even so, the highest percentage of smokers among any one group of athletes was 25.

Despite the enthusiasm for the arts of self-defense in public schools and universities none of the boxers or wrestlers came from the more highly educated sections of the community. Weight-lifters, marathon runners, and cyclists also came chiefly from the less educated sections. There was a more even spread among athletes participating in organized games.

Glutamic and Aspartic Acid Transaminase Activity.—The transaminases catalyze important reactions in the interconversion of amino acids and carbohydrate intermediates. It was therefore considered by Patrick and Tulloch that the activity of these enzymes might affect the rate of glyconeogenesis in the liver, and with this in mind they examined hepatic glutamic and aspartic acid transaminase activity in diabetic patients before and after treatment (*Lancet* 1:757, 1958). Liver biopsy specimens were obtained from 10 diabetic patients before treatment while they still had an elevated blood sugar level and glycosuria. The glutamic and aspartic acid transaminase activity of the liver specimens was estimated by the spectrophotometric measurement of the oxidation of reduced diphosphopyridine nucleoxide by oxaloacetate, which is a product of the transaminase reaction. The liver biopsy and enzyme estimations were repeated after the diabetes had been stabilized.

Despite wide variation in the transaminase activities from patient to patient, there was a statistically significant decrease in the transaminase activity after stabilization of the diabetes. This occurred regardless of the type of diabetes and whether control was achieved by dietary means or by therapy with insulin. There was no obvious relation between the initial transaminase activity and the type or duration of the diabetes, the weight of the patient, or the fasting blood sugar level. Nor was the change in the transaminase activity after treatment of the diabetes related to the fall in blood sugar level, the type of diabetes, the duration of treatment, or the amount of insulin required. Diabetic patients treated by diet alone showed a marked fall in the level of transaminase activity.

Blood Pressure in Newborn Infants.—Blood pressure in the neonatal period has been little studied largely because of technical difficulties. Ashworth and co-workers designed a modified sphygmomanometer suitable for the visual recording of the blood pressure of newborn babies (*Lancet* 1:801, 1959). From a cuff made of polyvinyl sheeting inflated around the forearm the arterial pulsation is transmitted to a glass capillary tube containing an interrupted column of xylol, beyond which is a cushion of compressible air. The xylol can be moved against this by pressure changes within the cuff. Small changes in the volume or tension of the tissues in the forearm, such as those produced by pulsation of the arteries, cause characteristic movements of the beads of xylol in the capillary tube. Systolic pressures can be recorded at intervals of a few seconds, but the diastolic pressures cannot be accurately measured. The range of error is the same as that with the ordinary sphygmomanometer. In normal babies the systolic blood pressure drops significantly in the first day of life, probably due to the opening up of the pulmonary vascular bed with expansion of the lungs. The mean fall was found to be 32 mm. Hg (range 14 to 54 mm.). Clamping the umbilical cord had no immediate effect. In half the infants examined there was a delayed rise in systolic pressure after clamping the cord, reaching a peak in 2.5 to 13 minutes.

Mechanical Patient.—A mechanical patient is one of several new devices developed recently in the laboratories of the Royal College of Surgeons. These devices are symbols of a vigorous effort to make anesthesia more scientific. As was made clear in a recent manslaughter case anesthetists still sometimes have to test the gases they use by sniffing them. It is hoped that soon new monitoring devices will remove the guesswork from anesthesia. The human nose is a poor analyzer. It can tell you what is there, but not how much. Prof. Ronald Woolmer calls his mechanical patient Pneumonica or New-Monica. As time goes on he hopes to build increasing degrees of accuracy into it. Eventually the artificial patient will be able to absorb anesthetics like a real patient. Pneumonica is electrically operated. Electronics provide greater flexibility and precision of control.

Another new mechanical device is an automatic minute-volume recorder designed by Professor Woolmer. Its purpose is to measure and provide an immediate and continuous graphic record of the amount of gas entering the lungs when inhaled anesthetics are used. This new breathing meter was tested clinically with satisfactory results. Professor Woolmer and Mr. D. W. Hill, a physicist, are investigating the use of gas chromatography for the rapid analysis of gases breathed by anesthetized patients. Within five minutes the apparatus will give the anesthetist a record of the mixture inspired and expired by his patient. Hitherto there has been no satisfactory way of doing this.

Vital Statistics for 1958.—The annual report on the health of England and Wales for 1958 (Registrar General's Quarterly Returns for England and Wales, December 31, 1958, Her Majesty's Stationery Office, 1959.) shows a birth rate of 16.4 per 1,000, the highest since 1949 when it was 16.7. The death rate of 11.7 per 1,000 was slightly above that for the previous year (11.5 per 1,000). The death rates per million in the last three months of 1958 from influenza and pneumonia were 599 and 21 respectively, compared with 788 and 462 for 1957. Deaths from poliomyelitis, 75, were also down by more than 50%. Accidental deaths were slightly lower, at 3,998 for the last quarter of the year. Deaths from all forms of tuberculosis were slightly less in the first three quarters of last year than in the corresponding period of the previous year. The figures were 3,293 and 3,391 respectively. Mortality from lung cancer continued to rise, with a total of 19,807 deaths for the year. The rate for all forms of cancer was 2,333 per million men and 1,929 per million women, compared with 2,312 and 1,890 in 1957. It is alarming that there were 589 deaths from appendicitis in this period, an increase of 83 over the figure for 1957. Most infectious diseases continued to have low mortality. There were 16 deaths from whooping cough and 36 from measles.

Maternal mortality continued to show a downward trend. In the first nine months of 1958 maternal deaths from all causes were 247, compared with 267 for the same period in 1957. Maternal mortality was highest in Wales and in the northwestern and northern regions, most of which are heavily industrialized. It was lowest in the southern, eastern, and north Midland regions. The death rate of children under 1 year in England and Wales in the third quarter was 20 per 1,000 live births. In June, 1958, the estimated population of England and Wales was 45,244,000.

Protection Against Pertussis.—The Whooping Cough Immunization Committee of the Medical Research Council (MRC) reported that with new pertussis vaccines it is possible to produce a high degree of protection against the disease (*Brit. M. J.* 1:994, 1959). The ability of a vaccine to protect mice against intracerebral pertussis correlated well with with the protection given to young children. In consequence it was recommended that only those vaccines which could be shown by the mouse protection test to be sufficiently potent should be released for human vaccination.

In the latest trials a new group of vaccines was tested, including an antigenic fraction, V_{17}, prepared according to the method of Pillemer and coworkers of Western Reserve University. This was obtained from Hemophilus pertussis by subjecting it to sonic vibrations of high frequency. The results of a trial on 4,500 children with Pillemer's antigenic fraction showed that it induced a high degree of immunity. It also produced an agglutinin response in mice and children less than that produced by whole bacterial vaccines with equally good protective power. It is therefore clear that although agglutinin production may sometimes, particularly with whole bacterial vaccines, parallel protective activity in children, this is not always so. The MRC group therefore considered that the mouse protection test was the most satisfactory means of assessing prophylactic activity.

Pillemer's antigenic fraction was compared with a whole bacterial vaccine in Liverpool children and found to be slightly more effective, although it caused more undesirable reactions, both local and general. This might have been due to its higher concentration. It was further shown that the protective action induced by a pertussis vaccine mixed with diphtheria toxoid was similar to that induced by the same pertussis vaccine alone. The most effective protection recorded in the trials reduced the attack rate in the inoculated to 4% of that in the uninoculated children. In general a reduction of about 10%, or a 90% protection rate, may be expected. If pertussis immunization is widely applied it should reduce the disease in the next few years to a fraction of its present incidence.

CORRESPONDENCE

MOTOR VEHICLE TRAFFIC DEATH RATE

To the Editor:—In his excellent article on prevention of injuries in college athletics, in THE JOURNAL, March 28, 1959, page 1405, Thorndike writes: "Highway safety engineers have so far been unsuccessful in reducing the accident and death rate among our motoring public."

This is not true. The facts are available from many sources. One interesting source is the table on page 109 of "CAA Statistical Handbook of Civil Aviation," U. S. Department of Commerce Civil Aeronautics Administration, 1958 edition, obtainable from the Superintendent of Documents, Washington 25, D. C., at 55 cents a copy. The data in the table are from the National Safety Council. The table referred to shows a steady decline in the motor vehicle traffic death rate from a high of 4.7 deaths per 100 million passenger-miles in 1937 to 2.6 in 1957. This includes passenger automobiles and taxis. The rate for 1956 was 2.7 per 100 million passenger-miles.

At first glance this appears to be a small decrease, but figured as percentage decrease in death rate it is quite respectable. On this basis the passenger car and taxi passenger death rate for 1957 was 3.7% less than in 1956 and 45% less than in 1937. The corresponding passenger death rate for buses was far lower, being 0.24 in 1941 and only 0.13 in 1957. This demonstrates the gross error of Thorndike's statement.

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Los Angeles 15.

EVALUATION OF METHYLPHENIDATE

To the Editor:—I read with interest the article, "Double-Blind Evaluation of Methylphenidate (Ritalin) Hydrochloride" by Darvill, in THE JOURNAL, April 11, page 1739, because I am conducting a study of this drug in outpatient psychiatric patients, as an adjuvant to psychotherapy. The patients take the drug only once weekly, just prior to the psychotherapeutic interview. To date, I have spent about eight months experimenting with the dosage and the effect of the drug on various patients at various times. I have recently begun a double-blind study.

There are two important criticisms of the above article that I would make. Darvill makes no allowances for the wide variety of effect of this drug. In some of my patients the drug produced a very pleasant effect, as if they were on "cloud nine"; in an almost equal number it precipitated anxiety symptoms and caused a rebound depressive hangover. It would be possible, therefore, for the number of those patients on whom it was helpful to be canceled out by the number of those whose symptoms were aggravated by the drug. I have no way to predict, as yet, from clinical symptoms, what the patient's response will be to the drug. The second point concerns the variation in dosage. My usual effective dosage runs between 20 and 80 mg. in a single dose. Generally speaking, doses of a lower order produce an effect in only a few of the more sensitive patients. Some patients have found that 10 or 20 mg. produces a detectable effect for them, and some have even refused to continue taking the drug because of an unpleasant effect induced by this dosage. Others have reported no detectable effect from single doses of 80 mg.

I believe that evaluation of this drug would require a period of time for adjustment of each patient's dosage to an effective level and for screening out those who had undesirable effects from the drug. I suspect that after this had been done, the physiological effects of the drug would make a double-blind study difficult. The fact that a double-blind study was possible, with negative results, suggests that the drug was not used in adequate dosage.

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DETERMINATION OF ETHYL ALCOHOL LEVELS

To the Editor:—The article by Friedemann and Dubowski in THE JOURNAL, May 2, page 47, dealing with certain aspects of blood alcohol level determinations and alcoholic intoxication is excellent. Certain of the comments, however, deserve further critical evaluation. They imply that ethanol, isopropanol, and certain other volatile skin cleansers have a negligible effect on the alcohol content of blood drawn with their use. This is somewhat contrary to my observations. If the skin is allowed to dry thoroughly, it is obvious that no contamination can occur. A problem arises as to when the skin is thoroughly dried, before removing a blood specimen for analysis.

I have repeatedly observed that ethanol and isopropanol, used in their usual cleansing concentrations, under ordinary laboratory conditions prior to the removal of blood, will occasionally cause a marked contamination of the specimen, introducing a positive error of as much as 200 mg. of ethanol per 100 ml. of blood. This contamination is not constant with each specimen but varies and probably depends on the technique of venipuncture used. I have found absurdly high blood alcohol levels (in the light of the defendant's clinical condition) associated with alcohol cleansing agents. At other times, on control studies, the amount of alcohol found is not significant. I believe that a definite danger exists of falsely increasing the blood alcohol content when such agents are used, and rather than add a possible error into an already controversial situation, I prefer the use of aqueous cleansing agents. This also obviates needless courtroom discussion.

The estimation of the blood alcohol level in the cadaver may be of interest. Postmortem diffusion of alcohol from the intestinal tract does occur, and for this reason I prefer blood from an extremity, before any embalming process is started. Since the average embalming room is contaminated with alcohols and aldehydes, it is almost impossible adequately to clean an embalming fluid bottle for use as a blood container. I prefer the use of chemically clean vials.

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MEDICAL HYPNOSIS

To the Editor:—In Dr. Erickson's letter in The Journal, Feb. 14, page 746, there are issues of fact and implication about the American Board of Medical Hypnosis which require correction and clarification. Dr. Erickson stated that this board was "organized by private individuals." The American Board of Medical Hypnosis is a division of the American Board of Clinical Hypnosis which has divisions also in psychology and dentistry and which is incorporated in the state of New York. The American Board of Medical Hypnosis is sponsored by the Society for Clinical and Experimental Hypnosis, the representative scientific organization in this field since 1949. The board is affiliated with the Institute for Research in Hypnosis, also incorporated in the state of New York. Leading members of the Society for Clinical and Experimental Hypnosis served individually as special consultants to the Council on Mental Health in connection with the 1958 Report on Medical Use of Hypnosis.

Dr. Erickson questions this board on the ground that hypnosis is "not a specialty," apparently implying that this board attempts to establish it as such. The fact is that the American Board of Medical Hypnosis opposes any limitation of practice to the use of hypnotic methods alone.

At its inception the American Board of Medical Hypnosis established contact with the secretary of the Council on Medical Education and Hospitals and with the secretary of the Advisory Board for Medical Specialties. Their advice was enlisted in the hope that the board would eventually qualify for functioning under A. M. A. auspices.

One requirement for recognition by the American Board of Medical Hypnosis is prior certification by one of the American medical specialty boards approved by the Council on Medical Education and Hospitals and the Advisory Board for Medical Specialties or active membership in the American Academy of General Practice. Should it develop that the structure of the hypnosis board be too atypical for operation among the basic specialty boards, it may still be hoped that the American Medical Association will accept the board's special status and cooperate in its functioning as an indication of interest and resolve to support high level education and practice in this area.

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To the Editor:—Dr. Schneck does not dispute the fact that the American Board of Medical Hypnosis and its sister boards were privately organized. Instead, he states, that the board is incorporated in New York state. Inquiry into this incorporation elicited, in December, 1958, the following telegram:

> The Commissioner of Education has indicated that he would consent to the incorporation of The American Board of Clinical Hypnosis, Incorporated, under the membership corporation law. Consent to incorporation does not carry with it any approval of the purposes of the corporation.
>
> Charles A. Brind, Counsel
> New York State Education Department
> New York.

Dr. Schneck states that the boards are sponsored by the Society for Clinical and Experimental Hypnosis and that they are affiliated with the Institute for Research in Hypnosis. The fact is, the boards were first announced to the membership of the society as an accomplished fact, fully organized, incorporated and ready to do business on a fee basis. This announcement was the first knowledge that the society membership had of the so-called boards. Hence, the society not only did not sponsor their organization but the matter of the boards was not presented to the membership of the society at the annual meeting in October, 1958. The constitution of the society provides that only the membership of the society, gathered in meeting, can transact society business. Therefore, no group within the society could actually sponsor the boards. While the assertion that the board is affiliated with the Institute for Research in Hypnosis is undoubtedly true, the institute is a privately organized and privately directed organization.

Since Dr. Schneck states that correspondence was established with the American Medical Association in organizing the boards, the following announcement in the *AMA News*, March 23, 1959, seems pertinent: "The AMA's Council on Mental Health announces that the 'American Board of Medical Hypnosis,' which presumably has set itself up as a certifying body for physicians using the technique, is neither connected with nor approved by AMA."

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MEDICOLEGAL ABSTRACTS

Criminal Insanity: Addict Suffering from Symptoms of Narcotic Withdrawal.—The defendant was found guilty of first-degree murder committed during the perpetration of a robbery. From a judgment imposing the death penalty he appealed to the Supreme Court of New Jersey.

The defendant offered the defense of insanity. The evidence, said the court, would well warrant a finding that the defendant was addicted to heroin, taking daily injections. The thesis of the defense was that the holdup was conceived and executed to acquire funds to purchase heroin to satisfy the imperative bodily demand for the drug while the defendant was in the withdrawal stage of his addiction, and hence he should be acquitted.

One of the medical specialists who testified on behalf of the defendant said that, during the withdrawal stage, the physical and emotional symptoms increase to the point of desperation, so that the addict's ability to reason things through is not nearly as logical as it normally is; hence he is quite ill, mentally and emotionally. It is probably true, he said, that addicts labor under a defect of reasoning because of these physical and emotional symptoms, and they are therefore less able to know the quality of the act they are doing. The witness agreed, however, that the defendant was not insane in the sense contained in the M'Naghten rule; he could distinguish right from wrong, but the withdrawal experience made him emotionally ill to a degree that colored his ability to do this. Finally, the doctor testified that drug addiction over a period of years may cause a certain amount of mental deterioration, although he did not suggest that any had here occurred. Nor was there testimony that the defendant was "insane" in any sense as of the time of trial.

The defendant's other medical expert stated that although the addict knows what he is doing the demand for the drug is so great that he cannot exercise judgment and restraint on his behavior to the same degree that a normal person can. He agreed that the defendant knew the difference between right and wrong, knew that what he did was wrong and a violation of the law, and was able to form the intent to rob, but, he said, "These people are no longer free agents. The need of the drug controls them."

The defendant's testimony, although descriptive of the painful withdrawal symptoms, revealed a clear appreciation and recollection of the crime. He recounted the planning and perpetration of the robbery and attack in detail.

On this record the trial court charged that voluntary use of narcotics will not excuse or justify a crime; that if such use results in a mental disease, the disease will receive the same recognition as insanity arising out of any other cause; and that where, as here, the claim is temporary insanity the issue is whether the accused was laboring under a defect of reason and did not know the nature and quality of the act he was committing, or, if he did know it, that he did not know what he was doing was wrong. Thus the issue went to the jury, in terms of the M'Naghten test applied to a temporary mental derangement. Defendant urged the restless question whether the M'Naghten rule is a correct approach to the defense of insanity. We fail to see how this case presents the question, said the Supreme Court, because the competing tests all require some form of mental disease or defect and none appears in the record before us.

The general rule, continued the court, is that the voluntary use of drugs, like the voluntary use of alcohol, is not a defense to murder (in the absence of mental disease resulting therefrom), although in some situations it may be pertinent with respect to the degree of that crime by negating the existence of the specific intent to kill. Our cases hold that voluntary intoxication is no defense to murder, but where the state's thesis is that the killing was willful, deliberate, and premeditated, intoxication which so prostrates the faculties as to prevent the formation of the specific intent to kill will hold the crime to murder in the second degree. The same rule applies with respect to the influence of narcotics.

Here the trial court directed the jury to consider the evidence offered as to insanity in determining whether there existed the specific intent to rob and directed an acquittal if that intent was not found. Since the defendant testified that he knowingly planned and committed the holdup, and in view of the testimony of the defense psychiatrists that the defendant did formulate the intent to rob, the jury was justified in finding as it did.

The court held, therefore, that the instructions on this part of the case were not grounds for reversal. The verdict was reversed on other grounds, however. *State v. White, 142 A (2) 65 (N. J., 1958).*

Privileged Communications: Waiver by Delay in Objecting to Testimony.—The defendant was charged with the crime of gross indecency. He was found to be a criminal sexual psychopath and appealed to the Supreme Court of Michigan.

During the course of the hearing the trial judge appointed a panel of three psychiatrists to determine whether he was a criminal sexual psychopath, one of the panel members being the defendant's private physician. The report of the panel was based largely on the notes and records gathered by this physician during his consultations.

The only issue on appeal was the defendant's claim that the entire examination was in violation of the doctor-patient privilege applying to communications between the defendant and his physician and was thus in violation of the defendant's constitutional rights. The defendant reasoned that he went to his physician voluntarily and in the ordinary doctor-patient relationship, and that his physician was therefore disqualified from serving as one of the three examining court-appointed psychiatrists, because he could not do so without necessarily making use of confidential communications made to him during the course of defendant's private treatment. The state admitted that the physician did make extensive use of notes taken by him in the course of private treatment, as well as of hospital records made in connection therewith. If disclosure of the confidential communications to the other psychiatrists was improperly made, said the court, there can be no question but what it influenced the opinion of the other members of the panel and was probably largely determinative of their final opinion. In any case, the court could not unravel the extent to which they may have been so influenced.

Whether or not the doctor-patient privilege was waived was of critical importance. The defendant knew the identity of the three psychiatrists appointed by the court to examine him and he therefore knew that his private psychiatrist was among their number. The state contended that because he made no objection prior to the hearing he waived any privilege which he might otherwise be entitled to claim as regards his own doctor's participation. However, said the Supreme Court, this court is of the opinion that the defendant was under no obligation, prior to trial, to raise objections to the appointment of a panel of psychiatrists, and therefore his objection at trial to the testimony of the psychiatrists on the grounds that they were of necessity based in part on confidential communication was timely. There does not appear to have been any waiver of his privilege.

Since the privilege had not been waived, the conviction based on it could not be sustained. The judgment against the defendant was therefore reversed. *People v. Wasker, 91 N. W. (2d) 866 (Mich., 1958).*

Medical Associations: Subpoena of Records.—This was basically an action for damages by the petitioner against the Los Angeles County Medical Association, and others. During the course of the proceedings the petitioner caused a *subpoena duces tecum* to be issued to the secretary-treasurer of the association, who refused to produce the documents requested. The trial court sustained this refusal so the petitioner filed a mandamus proceeding to compel the court to set aside its ruling. The mandamus proceeding was heard in the district court of appeal.

The petitioner had affirmatively alleged that the defendants conspired and combined to dominate and control the practice of medicine in Los Angeles County in such a manner as to prevent competition between licensed doctors in the area and its members, particularly when the licensed doctor came from out of the state. He had been a member of the medical association in another state prior to moving to California and alleged that his professional and ethical qualifications were of the highest caliber. He was denied membership in the defendant society, however, and, because of not being a member of the defendant, he was denied membership on the staffs of 90% of the hospitals in the Los Angeles County area.

The subpoena which the petitioner caused to be issued to the defendant requested its secretary-treasurer to produce all letters written by any member of the defendant regarding the petitioner; all investigations regarding the professional, personal, ethical, or moral background of the petitioner; all documents presented at any meeting of the defendant with reference to the petitioner's membership application; and all books, documents, records, papers, and files of the defendant in connection with its deliberations on the petitioner's membership application. On advice of counsel the defendant's secretary-treasurer refused to answer questions put to him concerning the rules, regulations, or policies of the association and refused to produce any of the material requested.

The question first arose as to the permissible limits of the taking of testimony by ancillary proceedings. The California law relating to this subject provides, in part, ". . . it is not ground for objection that the testimony will be inadmissible at the trial if the testimony sought appears reasonably calculated to lead to the discovery of admissible evidence. All matters which are privileged against disclosure upon the trial under the law of this State are privileged against disclosure through any discovery procedure. . . ." In the light of this rule the court of appeals said that it is evident that unless the matters sought to be elicited by the refused questions are privileged against disclosure under the law of this state, the questions should be answered.

The plaintiff, said the court, is seeking damages for injuries caused to him by the tortious conduct of defendants. He is not seeking, either directly or indirectly, to compel the defendant association to admit him to membership. It is the plaintiff's theory that the alleged practices of the defendant association, particularly those respecting the use of hospitals and the cooperation and consultation of member doctors of medicine with nonmember doctors of medicine, have been calculated to make it impossible for a nonmember to compete with a member of the association in the practice of medicine. Thus, the basic issue presented by the pleadings is the existence or nonexistence of a combination to restrain competition by the plaintiff.

The California law relating to statutory privileges provides against the examining of a witness about confidential communications between husband and wife, attorney and client, confessor and confessant, physician and patient, and public officers and certain newspaper personnel. In a prior California case it was indicated, in construing this provision, that unless the statute expressly extends the privilege to specific persons or classes, the law will not justify such individuals in refusing to disclose facts contained in documents which would otherwise be competent evidence in a particular proceeding. The court of appeals therefore concluded that the California law extended to the defendant no privilege against disclosure of the matters here in question.

The defendants argued, however, that public policy demands that documents, communications, and information of the nature and type sought herein should be treated as confidential and not available for disclosure and inspection as desired by the petitioner. More especially, they contend that since the courts will not interfere in the internal affairs of a voluntary association respecting applications for membership nor compel membership therein, questions or documents dealing with the reasons for petitioner's denial of membership therein and related rules in general become immaterial and irrelevant. The cases cited by the defendants, however, failed to support the contention that inquiry into the reasons for denial of membership will be precluded where it is charged that membership was denied for the purpose of restraining trade and competition as a part of a conspiracy to restrain trade and competition, an unjustified concerted refusal to deal, and an unjustified interference with contractual and advantageous relationships.

On a review of all the evidence, the court of appeals found that the plaintiff sufficiently alleged a purpose on the part of the defendants to restrain competition by him, as well as acts done in pursuance to that purpose, to state a cause of action. Perhaps some of these acts could be proved by the plaintiff without the aid of discovery proceedings, but probably the motives and purposes of the defendants could never be. Unless the plaintiff is permitted to obtain answers to proper questions, he will be deprived of the means of obtaining in advance of the trial information concerning the issues as well as the means of producing the evidence necessary to sustain his action. A review of the questions which the defendants have refused to answer, concluded the court, brings us to the conclusion that the matters, facts, and information sought to be elicited thereby are not privileged against disclosure under the law of this state and are relevant as determined by the subject matter of the action and by the potential, as well as the actual, issues in the case.

Accordingly the order of the trial court was reversed and the defendants directed to answer the requested questions and produce the requested documents. *Tatkin v. Superior Court, 326 P (2) 201 (Calif., 1958).*

MEDICAL FILM REVIEWS

Never Alone: 16 mm., color, sound, showing time 28 minutes. Produced in 1958 by Camera Eye Productions, Los Angeles, for and procurable on loan from the American Cancer Society, 521 W. 57th St., New York 19.

"Never Alone" stresses the fact that the American Cancer Society is nothing more than a continuation of an American tradition: Americans have always banded together to build a neighbor's house or a barn; a pioneer in any field in the nation's history has never been alone; and today the volunteer—the pioneer in the fight against cancer—is not alone. The cancer patient, as well as the cancer researcher, is never alone. All are people who fight cancer with everything at their command. The film details the country-wide operations of the American Cancer Society and its 2 million volunteer workers. It takes the viewer into the lives of some of the 800,000 persons now alive who have been cured of cancer, and then into research laboratories where actual research scientists are seen at their work. The film also takes the audience to a meeting of the board of directors of the society as well as to the homes of patients who are being aided by the society's service program. This is a well-organized human interest picture. It has a warm personal touch which will appeal to most adult audiences, and it is both entertaining and informative. This film is recommended for showing to service clubs, parent-teacher association meetings, and any lay groups who are interested in learning how voluntary health agencies mobilize persons from all walks of life, in a common struggle against disease.

Catalog of Films on Pediatrics and Child Health

A new catalog of films on pediatrics and child health is now available from the American Medical Association Department of Medical Motion Pictures and Television. This catalog is the result of a long-term reviewing project by the Committee on Medical Education of the American Academy of Pediatrics and the Department of Medical Motion Pictures of the A. M. A. Each film title is accompanied by a short description, information necessary to determine its suitability for showings, and its source.

MEDICAL LITERATURE ABSTRACTS

INTERNAL MEDICINE

Gas-Analytical Studies in Severe Pneumonia: Observations During the 1957 Influenza Epidemic. H. Herzog, H. Staub and R. Richterich. Lancet 1:593-596 (March 21) 1959 [London].

Between September and December, 1957, 264 patients with severe Asian influenza were admitted to the University Hospital (Bürgerspital) in Basel, Switzerland. Of these, 125 had pulmonary complications, and 22 were dangerously ill and needed special therapeutic measures, such as tracheotomy and artifiical respiration; 12 of the 22 died. Autopsy records of 11 of the 12 patients were available and revealed as a striking and characteristic finding severe tracheobronchitis, often hemorrhagic and pseudomembranous. Blood for gas analysis had been obtained by puncture of the brachial artery from the 22 patients. In many of these patients an arterioalveolar carbon dioxide tension gradient was observed. Oxygen was used extensively to combat hypoxia. The oxygen saturation rose in all but 5 of the 22 patients above 65%. These 5, whose oxygen saturation remained below 65%, died; hypoxia was directly responsible for 1 death only, but it may have been a contributory cause for the other 4. If oxygen unsaturation persisted, with or without carbon dioxide retention, artificial respiration was begun. Some patients had severe long-continued hypoxia without the occurrence of signs of damage to brain, heart, or kidney. Congestive heart failure was a significant cause of death in 4 patients. The most important cause of death was irreversible cardiovascular collapse which occurred in 8 patients; it was associated with leukopenia in 6 of the 8 patients.

The reported observations showed the considerable advances in the treatment of respiratory failure, since most of the patients who died did not succumb to hypoxia. Nevertheless, the total number of deaths was still too high and may be reduced by better management. No potential bone-marrow depressants, such as amidopyrine derivatives, should be used. Fever should be treated by physical means, supplemented by innocuous antipyretics, such as aspirin. Unless contraindicated by congestive failure, fresh whole-blood transfusions should be given. Routine use of gammaglobulin seem justified. Exchange transfusions might be worth trying in desperate cases, with the dual purpose of removing toxic substances and correcting the leukopenia.

Aseptic Cavitation of Pseudotumors. J. Prignot and R. Van de Velde. J. franç. méd. et chir. thorac. 12:623-645 (no. 6) 1958 (In French) [Paris].

Aseptic cavities occurring in masses of silicotic pseudotumor have been the subject of several recent clinical and radiologic publications. The authors found cavities of this type in 22 miners afflicted with confluent or massive fibrosis. Occurring in older persons after long work in a strong concentration of dust, these aseptic cavitations were accompanied by expectoration of dust-discolored sputum. There was temporary alteration of the general state, as shown by fever, weight loss, and lack of appetite. Less noticeable auscultatory symptoms were sibilant or moist rales. Erythrocyte sedimentation rate was determined according to the Westergren technique; the average rate was 48.6 mm. per hour, but the dispersion of results was wide. The Middlebrook-Dubos test was usually negative. This is in contrast to the case of silicotuberculosis where the reaction is positive.

These cavitations frequently complicate a serious and rapidly progressing pneumoconiosis. In this series aseptic necrosis occurred with pneumoconiosis in 18 of the 22 patients. Cavities are frequently multiple; they are especially localized in the median and peripheral portions of the upper and middle pulmonary fields, usually in the upper lobes; their contours are at first very irregular and rather thick, but may ultimately become thin and smooth. These cavities frequently progress toward obliteration by filling, rarely toward occlusion by retraction.

The differentiation between aseptic cavitation and silicotuberculosis is important medically, socially, and psychologically. Therapy for tuberculosis may even be contraindicated for aseptic necrosis. Differentiation is based mainly on bacteriological examinations (negative homogeneizations, inoculation of the guinea pig). Macroscopic examinations of sputum furnish useful indexes for diagnosis. The black expectoration of aseptic necrosis is frequently devoid of purulent material as opposed to what is observed in silicotuberculosis. Also, the quantity of

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The place of publication of the periodicals appears in brackets preceding each abstract.

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expectoration decreases quickly as soon as the necrosis has attained its maximum volume. The expectoration in cavitary silicotuberculosis remains on the contrary, abundant, even when tuberculostatic drugs are administered. Alteration of general health is much less persistent in aseptic necrosis than in silicotuberculosis. An observation of reactivation of tuberculosis by aseptic necrosis and also some observations of the occurrence of aseptic cavitation in patients with bacteriologically confirmed massive silicotuberculosis are presented.

The possibility of the reactivation of former tuberculous lesions imposes frequent and regular bacteriological controls, especially during the period when the excavation is spreading. These reactivations are not frequent enough to justify the preventive administration of tuberculostatic drugs. The frequent alteration of the general state indicates a rest cure, while risks of intrapleural rupture of the cavities and of hemoptysis necessitate definitive abstention from all heavy work. Isolation of patients with cavitations without bacilli is not indicated. Exeresis is only exceptionally possible, because most frequently cavitations complicate progressive and already advanced pneumoconiosis, where cardiorespiratory function no longer allows any major intervention.

Problems Regarding Anticoagulation Therapy of Some Thromboembolic Disorders: A Contribution of Cases. G. Crolle, S. Bianco and G. Büchi. Minerva med. **50**:324-333 (Feb. 7) 1959 (In Italian) [Turin, Italy].

The authors report on the results obtained in the treatment with anticoagulants of 132 patients with thromboembolic disorders observed during a 5-year period. Sixty-two patients had myocardial infarction, 42 had thrombophlebitis, and 33 had thromboembolic manifestations in various locations. Anticoagulants had a markedly beneficial effect in 72.2% of the patients; clinically appreciable modifications were observed during the course of the disease in 8% of the patients; thromboembolic complications during the course of the treatment occurred in 2.9% of the patients, and hemorrhagic complications in 2.1%; 5.1% of the patients died. The most favorable results were obtained in the treatment of deep thrombophlebitis and in the treatment and prevention of pulmonary infarction. Anticoagulants had a favorable influence in patients with myocardial infarction, decreasing the percentage of deaths and checking especially the occurrence of extracardiac thromboembolic complications. The evolution of the disease in patients with chronic obliterative arteriopathy was notably reduced, or in some favorable cases halted, only after prolonged treatment.

The risk of hemorrhage can be minimized if before treatment with anticoagulants the patient is given an accurate clinical examination to make sure that he is not of a hemorrhagic diathesis or subject to disorders which are contraindications to treatment with anticoagulants. The dose of anticoagulant depends in each case on the clinical course of the disease. Emphasis is laid on the use of protamine sulfate and of vitamin K_1 in counteracting possible hemorrhagic complications that may result from the use of heparin or coumarin preparations

Serum Hepatitis from Whole Blood: Incidence and Relation to Source of Blood. C. M. Kunin. Am. J. M Sc. **237**:293-303 (March) 1959 [Philadelphia].

The studies described were undertaken in 2 Veterans Administration hospitals in the Boston area for the following reasons: (1) to determine the incidence of serum hepatitis during 1952-1957, (2) to compare this incidence with that reported in the literature by others, and (3) to determine the relation between an apparent increase in incidence of serum hepatitis noted in certain years and the purchas of whole blood from a particular commercial source The study was undertaken when the occurrence o 7 cases of serum hepatitis at one of the hospital in a single year caused concern as to the possibilit that the blood from this commercial source may hav been responsible. The study was extended to th other hospital in order to test this hypothesis fu ther. Criteria for inclusion of a case in the stud were (1) evidence that the patient received tran fusions of whole blood in the respective hospita within a period of 1½ to 6 months prior to the onse of jaundice, (2) evidence that the patient did no receive transfusions or injections of pooled plasm or human thrombin during the incubation perio and (3) clinical and laboratory evidence of hepatit when chemical damage, metastatic tumor, nutr tional disease, or contact with cases of infectiou hepatitis could not be implicated as the cause Since patients receive many medications durin their hospital stay, injections for therapeutic an diagnostic purposes could not be excluded as v hicles for the transmission of the serum hepatit virus.

In the West Roxbury VA Hospital the records o 19 patients with serum hepatitis were reviewed Thirteen of these patients met the criteria for i clusion in the study. In the Boston VA Hospital th records of 49 patients with serum hepatitis wer reviewed, and 24 met the criteria for inclusio in the study. The data obtained by the authors ind cate that blood derived from a single commercia source was responsible for a small but significantl higher incidence of hepatitis than that which o curred from other sources. Since this bank provide only 11% of all pints of blood used in both hospital its true potential for producing cases of serum hepa titis was largely masked. This finding, together wit the presence of 4 icteric pints in a single year's ship ment from the offending bank, indicates not onl that inadequate methods of donor screening were used but also that the population serving as donors for that bank may well have a higher than usual incidence of serum hepatitis. Obviously the policies of such a bank need to be reviewed.

Sarcoidosis: An Analysis of Forty-five Cases in a Large Military Hospital. E. P. Singer, M. M. Hensler and P. F. Flynn. Am. J. Med. 26:364-375 (March) 1959 [New York].

Forty-one men and 4 women with sarcoidosis, most of them between the ages of 20 and 30 years, were studied at the U. S. Air Force Hospital, Park Air Force Base, California. The diagnosis was established histologically in 40 patients, and in the other 5 the clinical picture was considered sufficiently characteristic to make the diagnosis. In most of the patients the course of the disease was relatively benign. Restrictive ventilatory defects were severe enough in 5 patients to warrant disability and medical discharge from the Air Force. Lymphadenopathy was the most prominent physical finding, occurring in 25 patients. Slit-lamp examination performed on 22 patients showed evidence of active or inactive granulomatous uveitis in 11. Ocular manifestations presented the most cogent reasons for steroid therapy. Three patients were medically separated from the Air Force for ocular disability; 2 of these continued to have active iritis and/or uveitis despite continuation of systemic administration of steroids, and the 3rd had unilateral blindness. Epididymitis was an unusual feature in 2 patients, and renal insufficiency with azotemia in 1.

Sarcoidosis is usually detected early in its course in military personnel, often when it is apparently asymptomatic, with the aid of a routine chest roentgenogram. Hilar adenopathy with or without parenchymal changes is the most common finding pointing to the diagnosis. The greatly increased incidence among Negroes was again noted, since 25 (61%) of the 41 men were Negroes. Except for respiratory and ocular complaints, the symptoms were vague. There was a paucity of physical signs, even lymph node enlargement not being specific. In addition to the abnormal chest roentgenogram showing most commonly bilateral hilar adenopathy with parenchymal involvement, other laboratory findings included hyperglobulinemia, hypercalcemia, and, not infrequently, leukopenia with relative lymphocytosis and eosinophilia.

Therapy of Acute Leukemia by Whole Body Irradiation and Bone Marrow Transplantation from an Identical Normal Twin. J. B. Atkinson, F. J. Mahoney, I. R. Schwartz and J. A. Hesch. Blood 14:228-234 (March) 1959 [New York].

The authors present the history of an 18-month-old girl who was hospitalized with a history of anorexia, tiredness, and pallor of 5 weeks' duration. The symptoms had increased in severity particularly during the 2 weeks prior to admission. A diagnosis of acute lymphoblastic leukemia was established on the basis of the findings in the peripheral blood when compared with the results of the aspiration biopsy of the bone marrow. Supportive therapy given prior to the establishment of the diagnosis had no effect on the leukemic picture. The patient had a twin sister who was well. The blood types of all members of the family were ascertained with regard to ABO, CDE, and MN groups, and it was found that the twins had exactly the same types. There was evidence that the twins were identical. The possibility of using irradiation followed by bone marrow transplantation from the identical twin was considered, and the consulting hematologist, radiotherapist, and attending pediatrician were of the opinion that this might offer more than the routine methods of therapy.

Total body irradiation was given in a prone "frog leg" position. Irradiation with 380 r (skin) or 225 r (tissue) quickly eliminated detectable "blastic" elements in both the peripheral blood and the bone marrow. Nausea and vomiting commenced within 15 minutes after completion of the irradiation and, together with elevated temperature, continued during the following 17 hours preceding the transplantation of bone marrow. Under general anesthesia, bone marrow was obtained from the normal twin. A total of 31 bone marrow aspirations were done, with an average volume of 1.3 cm. and a total volume of 40.3 cm. Each bone marrow aspirate was withdrawn into a siliconized syringe, containing 1 cc. of an anticoagulant, and immediately and separately given to the leukemic twin through a polyethylene cannulated anterior tibial vein. Random cell counts of the nucleated elements revealed an average of 65,800 per cubic millimeter of marrow aspirate. This average approximated 234×10^6 nucleated cells per kilogram of body weight for the recipient. Because of thrombocytopenia, the patient was given 70 cc. of whole fresh blood taken directly from a heparinized donor. After this the patient received no further blood transfusions.

After the transplantation the patient's appetite improved markedly. She was very active and ambulatory on the pediatric floor within one week of the irradiation and transplantation. Hair loss began on approximately the 17th day after irradiation. It reached a maximum in 24 days. The estimated loss was 20 to 30%. The patient was discharged from the hospital 5 weeks after the transplantation. At home she showed excellent appetite and normal interest and activity. Seven weeks subsequent to the transplantation the child began to have anorexia, listlessness, pallor, and fever. Eight weeks after the transplantation, examination of smears from the peripheral blood and the bone marrow revealed a relapse into an acute lymphoblastic picture. The patient was hospitalized and transfused. Prednisone therapy was initiated. An excellent response was obtained within 2 weeks, and therapy was continued. Four weeks later, refractoriness to corticoid therapy was manifest, and mercaptopurine therapy was initiated with good results. Seven weeks later the patient again entered an acute blastic phase, and hospitalization was required for transfusion. Amethopterin therapy was started, but response was not satisfactory. Readmission to the hospital was required one month later for transfusion and supportive care, and the child died with the manifestations of an acute leukemia refractory to all modalities of therapy 8 months after the initial irradiation and marrow transplantation.

This case proved that irradiation followed by marrow transplantation can induce a remission in acute leukemia. No information was gained about an immune response in this case in which isologous marrow from an identical twin was used. Isologous transplants will necessarily be limited, since few persons have isologous siblings. Experiments on animals suggested that possibly a better result regarding control of the leukemia may be obtained from the use of homologous marrow.

SURGERY

Occurrence of Painless Acute Surgical Disorders in Psychotic Patients. W. E. Marchand, B. Sarota, H. C. Marble and others. New England J. Med. 260:580-585 (March 19) 1959 [Boston].

The authors present data on the presence or absence of pain as a presenting symptom in 79 patients with acute perforated peptic ulcer, acute appendicitis, or fracture of the femur who were treated at the Veterans Administration Hospital in Bedford, Mass., between 1946 and 1958. Pain was found to be absent in 3 of 14 patients with acute perforated peptic ulcer, in 7 of 19 patients with acute appendicitis, and in 19 of 46 patients with fracture of the femur. To explain the frequency of painless acute surgical disorders in psychotic patients, the meaning of pain is believed to be lost to those patients, who are left nonresponsive to painful processes. It was found that the absence of pain as a presenting symptom occurred twice as frequently in the group over the age of 60. The clinical experience has shown that, in a decreasing order of frequency, the patient with an organic psychosis and the hebephrenic and catatonic schizophrenic patients stood out as those who most often did not offer complaints of pain. Furthermore, the intensity of pain inherent in a pathological state may play a part in determining the presence or absence of pain. It appears that the more intense the pain of any process, the more frequently a complaint of pain will be offered. This suggests that the loss of the meaning of pain in psychotic patients can be overcome if the intensity of the pain is severe enough. In the experience of the surgical service at the VA hospital the presence of a mental disorder has not resulted in a higher than usual surgical mortality. There were no deaths among patients treated for acute perforated ulcer or acute appendicitis, and the mortality in fracture of the femur was found to be no higher than that found in general hospitals dealing with nonpsychotic patients.

Surgical Treatment of Constrictive Pericarditis. P. Santy, P. Marion and J. Gravier. Maroc méd. 37:1235-1241 (Dec.) 1958 (In French) [Casablanca].

The 101 patients with constrictive pericarditis operated on by Santy or by Marion between 1938, when Santy performed his first pericardiectomy, and June 1, 1958, fall into 3 groups corresponding to the 3 anatomicoclinical types of the disease—calcific constrictive pericarditis (43 patients), fibrous constrictive pericarditis (30), and subacute constrictive epicardiopericarditis (28). Calcific constrictive pericarditis is a comparatively late form. None of the 43 patients in whom it was present was less than 20 years old, and the average age was 48, with the patient's symptoms dating from 5 years before the operation. The patients with fibrous constrictive pericarditis were younger than those with the calcific form of the disease; they averaged 25 years of age, and their first symptoms of beginning asystole had appeared 3 years before they were referred to the surgeon. The third type—epicardiopericarditis—is a new form that has been seen only since the introduction of specific antibiotic therapy for tuberculosis. The average age of the patients was 25 years, and their heart trouble was usually of comparatively short duration—8 months on the average since the onset of the initial pericarditis with effusion. The tuberculous origin of the condition can be proved by the anatomicopathological examination, culture, and inoculation in a high proportion of these cases (18 out of 25).

None of the patients in this series died during operation, but 5 of the early deaths occurred in patients who had suffered operative complications (parietal rupture of the heart, coronary injury). The early deaths, i. e., those that occurred between the day of operation and the 19th postoperative day, were due to cardiorespiratory failure (5), progressive anoxia (7), and suppurative mediastinitis (3). The mortality increases with the age of the patient; thus, it was 11% of those under 20, 17% of those aged 20 to 40, and 33% of those over 40. The anatomicoclinical type of the disease also has an important influence on the operative prognosis: subacute epicardiopericarditis had the lowest mortality (8%), even though the tuberculous lesions are still active in these patients. Fibrous constrictive pericarditis came next with a mortality rate of 20.5%, and calcific constrictive pericarditis, which appears in an older age group, had a rate of 28% (which may rise to 40% in patients with complete arrhythmia).

Classification of the late results in patients with a follow-up of at least one year showed 3 late deaths not directly due to asystole, and 9 functional failures (leading to death in 3 patients). A complete cure was obtained in 38 patients, and the condition of 6 was greatly improved. Three additional cures were secured by reoperation on patients in whom the late functional results of the first operation were poor. Thus, 41 (73%) of the 56 patients followed for at least one year obtained perfect results.

The Clinical Aspect of Middle Lobe Syndrome. H. J. Peiper. Arch. klin. Chir. 290:231-259 (no. 3) 1959 (In German) [Berlin].

The author reports on 21 patients with isolated atelectasis of the middle lobe of the right lung, associated with chronic inflammatory and fibrous changes of the parenchyma as a result of temporary or permanent bronchostenosis, who were studied at the surgical clinic of the University in Marburg, Germany, between 1952 and 1958. The bronchostenosis in these patients was caused by hyperplasia of lymph nodes or by a destructive bronchitis. In an additional 6 patients, atelectasis of the middle lobe of the right lung was simulated by a malignant tumor, i. e., carcinoma of the middle lobe in 4 patients and bronchial adenoma in 2. The term "middle lobe syndrome" should be used only for isolated atelectasis of the middle lobe of the right lung of inflammatory origin. The symptomatology of the middle lobe syndrome is not characteristic and corresponds to that of a chronic pulmonary disorder. Almost all the patients complained of chronic cough with varying expectoration. Hemoptysis occurred occasionally. Pain in the anterior region of the thorax occurred frequently. Dyspnea was rare. Differential diagnosis is difficult, and roentgenographic examination is decisive, although it may still happen that the picture of an atelectatic middle lobe may be erroneously interpreted as interlobar effusion, pleural adhesion, or tumor shadow.

Fourteen of the 21 patients were operated on, and 7 were treated conservatively. Of the 14 patients, 11 underwent lobectomy, 1 had a bilobectomy, 1 had a thoracotomy, and 1 had a bronchotomy with removal of foreign body. There was no operative death. The postoperative course of one patient was complicated by hydropneumothorax which was treated successfully with Monaldi's drainage. Follow-up examinations showed that the patients were doing well except for one who had undergone bilobectomy for bronchiectasis and who was readmitted to hospital for pneumonia of the remaining lobe. An active surgical approach should be attempted in all patients in whom a neoplasm can be definitely excluded or who present unequivocal signs of chronic pulmonary suppuration, bronchostenosis, bronchiectasis, abscess, or bronchial calculi.

Mortality Associated with Biliary Tract Disease: I. Comparison of Surgical and Medical Management. J. A. Sterling, S. Virabutr and R. Goldsmith. Am. J. Gastroenterol. 31:241-249 (March) 1959 [New York].

Of 4,308 patients who died at the Albert Einstein Medical Center in Philadelphia between 1947 and 1956, 106 died primarily because of biliary tract disease. Forty-three of these 106 patients were operated on for relief of biliary tract disease, and autopsy was done on 12 (28%) of the 43. Of the 63 patients who died without undergoing surgical treatment, autopsy was done on 16 (25%). Of the 43 patients operated on, 16 had chronic calculous cholecystitis. This was also present in 5 additional patients in whom the gallbladder had perforated. Five patients had carcinoma of the head of the pancreas, and 10 patients had carcinoma in the duodenal papilla, gallbladder, liver, and common bile duct. The remaining 7 patients had acute inflammatory hepatobiliary tract disease. Of these 43 patients, 28 had remediable disease in the biliary tract. In 3 cases death was ascribed to errors in surgical techniques. Seventeen patients had additional diseases and complications, including myocardial infarction, pulmonary emboli, duodenal ulcer, pancreatitis, acute appendicitis, gastrointestinal hemorrhage, diabetes mellitus, acute renal insufficiency, and primary tuberculosis. Except for the 8 patients with myocardial infarction, 20 patients (46%) with benign disease could have been saved.

Of the 63 patients not operated on, 13 had acute cholecystitis, and 2 had empyema of the gallbladder. Twenty-six of the 63 patients had carcinoma of the head of the pancreas or carcinoma in the common bile duct, liver, or other parts of the biliary tract and could not have been saved. Of the remaining 37 patients with benign disease, 11 had additional irremediable disease, leaving 26 (41%) in whom benign biliary tract disease was the cause for death. Thus, a total of 46 (43%) of the 106 deaths might have been prevented by the application of early surgical procedure and adequate management.

Adenomas of the Colon and Rectum. E. R. Wasemiller. Journal-Lancet 79:89-96 (March) 1959 [Minneapolis].

The literature on adenomas of the colon and rectum, which are the commonest benign tumors occurring in these parts of the large intestine, has been reviewed with respect to the basic concepts in causation, incidence, and pathogenesis of these tumors and the methods of diagnosis and treatment.

Proctosigmoidoscopic examinations were performed by the author on 200 patients as part of the routine physical examinations and because of the following symptoms indicating rectal or colonic disease: (1) bleeding or passing of mucus, (2) change in bowel habits, (3) tenesmus, (4) constipation, (5) diarrhea, (6) abdominal cramps or pain, and (7) hemorrhoids. These examinations revealed that 6 of the 200 patients had carcinomas, 42 had benign adenomas, 1 had an abscess, 2 had acute proctocolitis, and 2 had melanosis of the colon. Thus, 3% of the patients examined had carcinomas and 21% had benign adenomas. Of the 42 patients with adenomas, 26 had single, 16 had multiple, 2 had pedunculated, and 38 had sessile adenomas. There were 2 with villous adenomas. Six had adenomas above the 20-cm. level. The 21% incidence of adenoma was somewhat higher than the national average of about 10%. This was attributed to the fact that most of the patients examined were over 40 years of age and had symptoms indicating rectal or colonic disease.

It is now generally accepted that benign mucosal adenomas are definitely premalignant lesions and should, therefore, be treated adequately by local removal or destruction. In the reported series, adenomas above the peritoneal reflection were removed by cold biopsy forceps, and the base was coagulated only if necessary to control bleeding. In only one patient did a complication occur; he complained of lower abdominal pain the day after operation and had a temperature of 99.8 F (37.5 C). His symptoms subsided within 12 hours. Radical surgery is indicated if invasive carcinoma has developed. Early diagnosis, proper management, and careful follow-up are essential if prophylaxis of cancer of the large intestine is to be appreciably improved.

Tendon Transplantation in Poliomyelitic Complications of the Knee and of the Foot: Long-Term Results. V. Genta and M. Vacirca. *Arch. chir. ortop.* 23:349-369 (Nov.-Dec.) 1958 (In Italian) [Milan, Italy].

Transplantations of the biceps femoris to the knee and of the extensor digitorum longus to the foot were inspected in 48 patients in periods not earlier than 5 years after surgery. The operation aimed at stabilization of flexion of the knee or foot weakened by poliomyelitis. Transplantation of the biceps femoris alone was done in 9 instances, of semimembranosus alone in 1, and of sartorius combined with internal rectus in 1. Biceps femoris was combined with semitendinosus in 4 instances, with semimembranosus in 4, and with both semitendinosus and semimembranosus in 4. End-result of the correction of the knee flexion was poor in one patient, who still required orthopedic apparatus for walking and in whom flexion instability was attributed to postoperative complications. The remaining patients regained the functional stability of the knee. Of the postoperative complications, patellar dislocation developed in 7 instances, all being related to the transplantation of the biceps femoris alone. Recurvatum was observed in 10 instances of transplantation of the biceps femoris alone or in combination with other muscles. Of 30 foot operations, the end-result was good in 23 patients and poor in 7. The most effective transplantation was obtained with the extensor digitorum longus on the first metatarsal in paralysis of the tibial muscles and with peroneal muscles on the heel in paralysis of the tricipital.

Traumatic Pancreatitis. R. Amgwerd. Helvet. chir. acta 25:459-474 (Dec.) 1958 (In German) [Basel, Switzerland].

The author describes observations on 9 patients with traumatic injuries of the pancreas, who were treated in the surgical clinic of the University of Zurich between 1940 and 1957. Two were open and 7 were closed injuries. The diagnosis of this lesion in accident cases is difficult, particularly when injuries of the head or of the extremities exist in the same patient. Furthermore, other internal organs may be injured simultaneously, as was the case in 5 of the 9 patients. The traumatic injuries vary, depending on the intensity of the injuring force. Slight contusions are probably more frequent than is generally realized. Tearing may range from a small tear into the capsule to complete division of the pancreas. Mild traumas may cause edema or small hemorrhages into the gland. Traumatic pancreatitis which is accompanied by massive discharge of secretion into the free abdominal cavity produces increasing peritonism, whereas mild leakage of secretion may result in peritoneal adhesions, proliferation of connective tissue, and encapsulation of the omental bursa. Chemical tests on blood and urine may confirm the diagnosis of traumatic damage to the pancreas. The examination of the diastase content of the urine according to the method of Wohlgemuth is often sufficient. Observations on the carbohydrate metabolism are helpful in that hyperglycemia may be indicative of pancreatic injury.

The treatment of traumatic pancreatitis should aim at preventing massive absorption of pancreatic secretions and the autointoxication of the organism. Mild lesions heal spontaneously. Tears in the gland should be repaired by capsular suture. The author rejects the suture of a divided excretory duct, but advises internal splinting with the aid of a polyethylene catheter. Torn-off portions of the pancreas should be removed. Duodenopancreatectomy and observations on one of his own cases convinced the author that reduction of the pancreas by more than half does not result in incretory disturbances. Drainage is necessary in all operations on pancreatic wounds. Pancreatic pseudocysts develop when pancreatic secretion enters the closed omental bursa. Treatment consists in external drainage of the cyst (marsupialization), if possible in extirpation of the cyst, or in anastomosis of the cyst to a hollow organ. Fistulas, abscesses, and hemorrhages may develop as sequels of traumatic pancreatitis. The hemorrhages may be fatal. The author gained the impression that the prognosis of traumatic pancreatitis is determined by the severity of the pancreatic and of the accompanying injuries. In case of severe damage the destroyed tissue should be removed so as to prevent chronic pancreatitis.

Pilonidal Disease: Management without Excision. P. Jacobson. GP 19:84-90 (March) 1959 [Kansas City, Mo.].

One hundred eight patients with pilonidal disease were operated on according to a method devised in an attempt to preserve the normal anatomy of the sacrococcygeal region, and particularly of the intergluteal depression, since alteration of this depression, when it has been excised along with the pilonidal lesion, can be the cause of much discomfort, resulting in inability to take long automobile trips or to sit normally for extended periods. This method consists essentially of destroying the epithelium-lined channels and properly exposing the sinuses, all with a powerful electrosurgical unit. Low spinal or saddle block anesthesia is preferable to general anesthesia, although in some cases local block is sufficient. The wound is then treated as a burn and heals by granulation and epithelization. Meticulous attention to the details of controlling and directing the growth of epithelium down the slopes of the wound and preventing hairs and other foreign bodies from becoming buried is essential for success.

Of the 108 patients so treated, only one had a known recurrence. Seventy patients had simple cysts, of which only 6 were suitable for marsupialization. Thirty-three patients had accessory sinuses, and 6 had recurrent sinuses. Of the latter, 1 had 4 previous operations; 1, 3 operations; 1, 2 operations; and 2, 1 operation. The only patient who had a recurrent sinus in this series had been operated on only once; he was a large, fat, hairy 16-year-old boy. The author believes that, if proper precautions regarding the hair had been observed, there might have been no recurrence.

The method described returns the sacrococcygeal region to its normal state, and there have been no complaints of sensitiveness. Criticisms of this operation are that it is not a clean surgical procedure and that it requires long, tedious postoperative care. The author does not consider these criticisms to be valid if this additional burden overcomes the 3 objections to the excision operation, namely, the high recurrence rate, the long period of disability, and the unnecessary sacrifice of the median depression. He believes that the results obtained and the absence of sequelae which sometimes follow the excision operation, even when it is successful, have warranted all the extra effort.

Experiences with Bone Transplants Preserved by Deep Freezing. P. Buser. Arch. klin. Chir. 290:289-309 (no. 3) 1959 (In German) [Berlin].

The author reports on 127 patients in whom transplanting of 158 bone grafts, which had been preserved by deep freezing, was carried out at the surgical clinic of the canton hospital in Winterthur, Switzerland. Of the 127 patients, 37 had primary transplantations for recent bone injuries, 56 had transplantations for pseudarthroses of long bones, 20 had transplantations in the course of arthroereises of the Eden-Brun plastics type, and 14 had transplantations for pseudarthroses of the neck of the femur, arthrodeses, and stiffening of the spinal column. The bone transpants used were homoplastic cortical grafts.

The results were satisfactory in those patients in whom the grafts were transplanted into a bed which lent itself to active repair by a substitute in such a way that a firm union took place. The results were unsatisfactory in those patients in whom only slight union of the transplant with the host-bone occurred. The results thus were satisfactory in the patients with recent fractures, pseudarthroses of long bones, and arthrodeses. In the patients with arthroereises of the Eden-Brun type and in those with more extensive bone defects (defect pseudarthroses), the contact of the transplant with the host-bone was insufficient, and the results were similar to those obtained with transplantation of soft tissue, i. e., absorption took place. In the comparatively small number of patients with these lesions, the use of autografts covered by periosteum is indicated. In all the other patients the use of cortical transplants preserved by deep freezing proved to be satisfactory. The method of preservation is simple, and the duration of storage has no effect on the results of transplantation. Manifestations of intolerance were not observed in the recipients of bone transplants.

NEUROLOGY & PSYCHIATRY

Studies of Sleep Deprivation: Relationship to Schizophrenia. E. L. Bliss, L. D. Clark and C. D. West. A. M. A. Arch. Neurol. & Psychiat. 81:348-359 (March) 1959 [Chicago].

It is common knowledge that fatigued children and adults tend to be irritable and unreasonable. It is less commonly emphasized that many agitated persons on the brink of a psychotic break suffer from severe insomnia and that a few pass through a prolonged period of wakefulness as the schizophrenic process unfolds. Two examples are cited of patients who illustrate this situation. Both were racked with intense psychological pain and overwhelmed by seemingly unsoluble problems. Both failed to sleep for several days, emotionally isolated themselves, and became psychotic. In each case the schizophrenic episode was brief and recovery rapid. Either patient might have become schizophrenic without the additional insult of sleep deprivation, but it seems plausible that the insomnia may have been a critical factor in the process.

These clinical observations led the authors to postulate that sleep deprivation, although a consequence of emotional turmoil, may play a critical role in the precipitation of some psychoses. Therefore, studies were made in 7 normal medical students who remained without sleep for 72 consecutive hours. During this time they stayed in rooms on an open psychiatric ward, took their meals in the hospital cafeteria, and were free to stimulate wakefulness by whatever diversions they might choose. The experimental setting thus was permissive and anxiety-sparing. Changes on psychological tests which were administered to these students were insignificant, but behavioral and subjective alterations were considerable. Feelings of depersonalization, illusions, hallucinations, disturbances in time perception, and auditory changes were common. Despite the long period of wakefulness, adrenocortical activity remained normal.

A second study was made in 4 persons who had received lysergic acid diethylamide (LSD-25) without sleep deprivation on at least 4 previous occasions, and had not had perceptual disturbances (LSD-25 hallucinations). After being deprived of sleep for 48 hours, they were given small amounts of LSD-25. Hallucinations developed in all 4 persons under the combined influence of sleeplessness and the drug. Sleep deprivation thus markedly enhanced the ego-disruptive effects of LSD-25. Presumably this may have been due to an alteration in cerebral metabolism consequent to prolonged sleeplessness, which made the brain more susceptible to the "psychotomimetic" effects of LSD-25. It is suggested that sleep deprivation, when combined with isolation and incapacitating anxiety, may have a pathogenic potential that has not been adequately appreciated.

Chemopallidectomy. H. D. Paxton, D. T. Smith and R. S. Dow. Northwest Med. 58:370-372 (March) 1959 [Seattle].

The authors' experience with chemopallidectomy indicates that it has value in alleviation of rigidity and tremor of the extremities in patients with Parkinsonism. The indications and contraindications are emerging with experience. The procedure does not favorably influence those symptoms due to bulbar involvement and is contraindicated in the elderly patient with mental symptoms. It is of palliative value in patients with dystonia musculorum deformans and in the control of choreiform movements. It proved ineffective in athetosis and spasmodic torticollis in a limited number of patients.

Clinical Aspects of Tropical Ataxic Neuropathies Related to Malnutrition. G. L. Money. West African M. J. 8:3-17 (Feb.) 1959 [Ibadan, Nigeria].

Apart from the dietary neuropathies related to beriberi and pellagra, there are a number of "nutritional neuropathies of obscure origin." The present paper deals with cord neuropathies in which the outstanding clinical feature is ataxia. Ataxic neuropathies have been reported from Jamaica, Nyasaland, Sierra Leone, the Seychelles, Ceylon, Nigeria, and Liberia. During World War II similar neuropathies were observed in prisoners of war, and were related to deficiencies of factors of the vitamin B complex. The finding of an endemic focus of neuropathy in a district of southern Nigeria provided an opportunity to reexamine the relationship of these neuropathies to malnutrition. This report is concerned with the clinical aspects observed in 100 patients (40 males and 60 females) with severe ataxic neuropathy. Twenty-two of the patients were observed by the author between 1954 and 1956 in the University College Hospital in Ibadan, western Nigeria; the rest were studied in their villages.

The hospital patients were investigated for an average of about 8 weeks and, on discharge, were followed up for varying periods, up to 18 months, in the outpatient department. Dietary supplements were given to the hospital patients—milk, brewer's yeast, orally administered multivitamin preparations, and parenterally administered preparations of thiamine, cyanocobalamin, and vitamin mixtures. A common residence was of greater etiological importance than "blood" relationship, i. e., genetic factors. A history of repeated episodes of angular stomatitis, glossitis, or scrotal dermatitis was obtained from 96% of the subjects. Scrotal dermatitis was observed in 27 of the 40 males. The combination of mucocutaneous lesions with visual blurring ("oculo-orogenital syndrome") was associated in 2 of the patients with onset of cord symptoms. Cheilosis, blepharitis, and conjunctivitis were also observed.

Superficial sensory disturbances in the legs were the earliest manifestations in this series, and they preceded ataxia by weeks, months, or even years. Pains and paresthesias preceded ataxia in 99% of the patients. Pains and burning feet were present in 36% and were identical with the painful feet syndrome. Impairment or loss of joint position sense and vibration sense was the characteristic sensory finding; 82% of the patients showed loss or impairment of joint position sense in the toes, ankles, knees, and hips. In the mildest cases only the toes were affected, but in the severe cases with ataxic paraplegia there was complete loss of appreciation of passive movements up to and including the hips. Similar but milder changes were found in the upper limbs. Disturbance of gait was the yardstick of selection of this group of 100 cases. In 75 patients ataxia of gait was obvious; in 25 others there was clumsiness with ataxia on closer examination, especially on toeing the line. Loss of libido and impotence were frequent complaints in severe ataxic neuropathy. The circulation in the legs appeared sluggish in advanced neuropathy, and the limbs were cold to touch. Transient or persisting blurring of vision was observed in 87% of the patients; defective hearing, in 25%. Motor power was surprisingly well preserved. The symptoms and signs point to an affection of the first sensory neuron—the posterior root ganglion with its (peripheral nerve) and central (posterior column of spinal cord) processes.

Exacerbations of symptoms in the rainy season may be due to the "hungry season" and the metabolic demands resulting from increased malaria, typhoid, and other infections. A simple nutritional or metabolic explanation does not fit all the facts. The incidence of mild sensory disturbances and mucocutaneous lesions is high in the second decade of life, but the peak of onset of neuropathy is in the third decade for women and the fourth decade for men; these neuropathies are absent in the first decade when the most dramatic disorders of malnutrition, such as kwashiorkor, occur. The effects of treatment with adequate diets, reinforced with vitamins, are disappointing in established cases. This is particularly striking when one considers how easily the milder sensory disturbances and mucocutaneous lesions disappear on brewer's yeast. On the basis of this clinical study, malnutrition appears to be important in the etiology of these neuropathies. A search must be made for toxic antimetabolites, for it is possible that in some cases an additional injury is responsible for the neurological disorder.

Quinacrine and Chloroquine in Treatment of "Petit Mal" Epilepsy: Preliminary Report. H. J. Vázquez, N. Hojman and F. E. Quiroga. Semana méd. 66:92-94 (Jan. 15) 1959 (In Spanish) [Buenos Aires].

Good results from the administration of either quinacrine or chloroquine for the control of mild epilepsy have been reported in the literature. The results in epilepsy were unexpected, as the drug had been given to epileptic children for the treatment of intestinal parasitosis. The authors resorted to this therapy in 13 children, between the ages of 2 and 14 years, with petit mal epilepsy; none of the patients had intestinal parasitosis. Epilepsy had lasted for 8 months in the infant and between 3 and 8 years in the older children. The attacks developed in association with loss of consciousness in 11 patients and with akinesia in 2. Five of the patients had asphyxia and cyanosis at birth, 2 had cranial trauma once or twice, 4 belonged to families with epileptic members, and 2 had several clinical forms of epilepsy in association. In a 12-year-old patient, the disease had changed to grand mal epilepsy at the age of 11 years. The IQ was normal in 11 patients and was lower in 2 (61 and 56% respectively). The electroencephalograms had the typical tracings of petit mal epilepsy in 11 children. The classical treatment with anticonvulsants had failed in 10 patients. Three patients had had no previous treatment.

Either quinacrine or chloroquine, alone or in association with other anticonvulsants, was given to the patients in this series in daily doses of 200 mg. for 10 consecutive days. The daily dosage was given in 2 fractions of 100 mg. each at 4-hour intervals. In all patients the epileptic attacks ceased within 2 or 3 days from the start of treatment, and the electroencephalograms became normal. In the majority of the patients the attacks did not reappear after discontinuation of the treatment, and in the few in whom they did reappear, quinacrine was given once a week for several weeks. The satisfactory results obtained in all the patients have been sustained in a follow-up of 4 months to 2 years.

The authors conclude that quinacrine and chloroquine are anticonvulsive drugs of great value. The disappearance of the epileptic attacks and the normalization of the electroencephalograms of the patients in this series have never before been observed in patients having any other treatment for epilepsy.

Neurological Aspects of Mexican Mushrooms Causing Hallucinations. A. Ortiz Galván and M. Baldwin. Rev. méd. hosp. gen. 22:137-150 (Feb.) 1959 (In Spanish) [Mexico, D. F.].

Since Aztec times mushrooms of several varieties of the Psylocibe genus have been the commonest intoxicating mushrooms in Mexico. Ingestion of these mushrooms or of psylocibin, their active principle, produces disorders of behavior and a complete but transient psychosis without any sequelae. These disorders are equal to those caused by the chewing of mescal buttons or by the ingestion of either bufotenin or diethylamide of lysergic acid.

Observations regarding the intoxicating effects of Psylocibe mushrooms were carried out on a normal man and on 5 adult chimpanzees. The man was given 12 Gm. of mushrooms (dried by heat). He exhibited moderate symptoms, consisting of color hallucinations, mydriasis, hyperthermia, hypertension, muscular hypotonicity, marked introversion, hostility toward persons about him, and loss of notion of time for 3 hours. In the monkeys the first symptoms appeared within 15 minutes after administration of the intoxicating substance and lasted for 1 or 2 hours. A dosage of 20 Gm. of mushrooms given to an intact chimpanzee made it passive and tame for 45 minutes, after which it returned to normal behavior; there were no marked neurological symptoms. A dosage of the extract, equivalent to 40 Gm. of mushrooms, was simultaneously given to 2 intact chimpanzees and to 1 chimpanzee which had previously been subjected to bilateral temporal lobectomy. Both intact animals exhibited mydriasis and signs of muscular hypotonicity and were tame and entirely passive for about 45 minutes; after that they became violent, impatient, and desperate, striking themselves against their cages and not returning to normal behavior for an hour. No intoxicating effects were produced in the animal which had previously been subjected to bilateral lobectomy. In the third animal experiment a dosage of the extract, equivalent to 50 Gm. of mushrooms, was placed by intubation in the stomach of an intact chimpanzee while it was relaxed with succinylcholine. The rectal, gastric, and esophageal temperatures did not change, but the arterial pressure increased. The electroencephalogram remained normal, its tracing showing that stimulation by pain and noise produced no change.

The experiments show that Psylocibe mushrooms act on the central nervous system of both man and intact animals, but they do not produce any intoxicating effect in an animal which has previously undergone bilateral temporal lobectomy. The behavioral and mental disorders caused by ingestion of these mushrooms are the same as the symptoms characterizing epilepsy. This is due to the lesion of the temporal lobe which seems to be the area of cortical association with the hypothalamic and subcortical centers. The latter are involved in the neurological mechanism of epilepsy and in the psychophysiological mechanism of mental disorders caused by psychogenetic substances.

GYNECOLOGY & OBSTETRICS

The Association of Bladder Disturbances with Chronic Cervicitis. G. S. Foster. J. Obst. & Gynaec. Brit. Emp. 66:47-50 (Feb.) 1959 [London].

An infected cervix is frequently associated with inflammatory disturbances of the urinary tract and may be incriminated as the primary focus of infection. After citing earlier reports on this problem, the author says that it was noted in an initial survey that approximately 10% of the women with cervicitis, attending the gynecologic outpatient department of Cardiff Royal Infirmary, had troublesome urinary complaints. Sixty-five consecutive cases of this type form the basis of this study. These women were submitted to a thorough gynecologic and urologic examination and, after treatment of the infected cervix, were observed for a minimum period of 2 years. Cases complicated by vulvitis, urethral caruncle, cystocele, etc., were excluded from this survey. Thirty-three of the 65 women in whom cervicitis was associated with disturbances in micturition were found to have what may be termed cervicotrigonitis, in which cervicitis is accompanied by certain changes in the bladder mucosa, particularly in the trigonal area. Though well-defined inflammatory changes are rarely demonstrable in cervical erosions, the hyperactivity of the cervical glands and hyperemia seem to influence the function and anatomy of the bladder base. Cauterization of the cervix was successful in relieving the urinary symptoms in 48 of the 65 patients. The state of the bladder mucosa seemed to be the main factor in the success of the treatment.

The author found that bladder symptoms may exist in cervicitis without mucosal changes in the bladder, and in these cases appropriate treatment of the infected cervix may be expected to cure the urinary symptoms. The relatively few patients who were not relieved were subsequently cured by urethral dilatation. In the presence of trigonitis, the response to cauterization of the cervix was less satisfactory, and the condition of more than a third of the patients was not improved. Neither did these patients respond to urethral dilatation.

The Place of Vaginal Smears in Indications and Dosage of Complementary Androgen Therapy in Breast Cancer. A. Sicard and C. Marsan. Presse méd. 67:363-366 (Feb. 25) 1959 (In French) [Paris].

In order to define indications and dosage of androgen therapy, vaginal smears were routinely obtained from 62 patients with breast cancer, ranging in age from 40 to 79 years, who were followed up for several years. The investigation revealed that the effect of treatment depends on the regular administration of a sufficient quantity of androgen for a prolonged period. Hormone therapy must be individualized; the dosage which is inadequate in one patient may be unnecessarily virilizing in another.

The usual treatment consisted of 3 series of 10 injections of 100 mg. of testosterone propionate per year. The difficulties sometimes encountered in persuading patients to persevere in this therapy made the implantation of a single dose of hormone at the time of surgical intervention preferable in some patients. Reimplant can be carried out every 6 months or every year. The 2 treatments can also be continued by implantation during the operation and maintenance thereafter with intramuscular injections. When testosterone was administered in sufficient doses, the vaginal smears usually showed an androgenic apearance in menopausal women, and an atrophic appearance in those who were still menstruating. The androgenic appearance of the smears was not constant; its absence, however, does not justify the conclusion that treatment was ineffective. In some cases the smears were frankly estrogenic. Many theories have been advanced to explain this phenomenon, but none is satisfactory. Therefore, the specificity of an "androgenic" smear cannot be positively affirmed. It seems possible, however, to conclude that typical androgenic smears indicate a definite and sufficient male hormone activity, but a nonandrogenic smear does not necessarily indicate the absence of male hormonal activity. The percentage of androgenic cells cannot be accepted as a quantitative test of androgynism.

As for the problem of the complementary treatment of patients with cancer of the breast, dense or atrophic smears in menopausal women should lead to adoption of the same therapeutic attitude as do androgenic smears. This study shows that it is illusory to try to establish a standard hormonal dosage to produce castration. The dosage required depends on several factors, including the initial state, the method of administration, and the individual constitutional state of the patient, which can only be determined by prolonged clinical and cytological observation.

Prolonged Pregnancy: Its Hazards and Management. I. Cope. M. J. Australia 1:196-202 (Feb. 7) 1959 [Sydney].

The records of all women who were delivered at the Royal Hospital for Women, Sydney, 297 or more days after the first day of the last menstrual period, between 1947 and 1952, were examined. Survey of a total of 19,475 deliveries revealed 2,013 in which delivery was delayed beyond 297 days, but 463 of these were disregarded in the further studies, either because there was evidence of gross menstrual irregularity, or because of uncertainty about the date of the last menstrual period. Thus, there remained 1,550 cases for analysis. Analysis of the relationship between prolonged pregnancy and maternal age revealed a higher incidence of prolonged pregnancy in the younger age groups, but this is more apparent than real because of the higher rate of induction of labor in older women and the slightly longer menstrual cycles in the younger women. Parity seemed to play no significant part in prolonged pregnancy, while 41% of those whose pregnancy was prolonged were primigravidas; the latter also accounted for 39.2% of the total number of deliveries. In 77 women in whom the periods of gestation for siblings (of the delayed-delivery infant) were known, the average gestation time in these 77 other pregnancies was 281.8 days; this deviates only slightly from the normal average of 282.5 days for Australian women.

Many cases of prolonged pregnancy do not involve any special difficulty or greater risk than pregnancies of normal duration. This series of cases showed that there are increased difficulties at delivery, and also that the risk of fetal death from "unexplained" anoxia increased significantly after the 40th week. This agrees with the observations made by others. However, the author points out that only 62 of 1,550 infants were lost in this series after the 296th day. The risk to the fetus increased with maternal age, and it was greater in primigravidas than in multigravidas, although in this series trauma associated with internal version and breech extraction of a large fetus increased the dangers to the fetuses of multiparas. It is significant that, almost without exception, some other complication of pregnancy was present in the cases in which stillbirth occurred.

The use of surgical induction of labor is of limited value in prolonged pregnancy. In this connection the author points out that at Hammersmith Postgraduate Hospital, London, there were 3 stillbirths and 1 neonatal death in 155 cases in which labor was induced surgically for prolonged pregnancy. This fetal loss was only slightly less than if inductions of labor had not been carried out. If a safe method of induction of labor was available, this could be carried out in all cases; but selective induction of labor is suggested for women with prolonged pregnancies at greater risk—the older women and the women with hypertension or preeclampsia. However, not all infants will be saved from placental insufficiency by induction of labor.

"Normal Midwifery." T. B. FitzGerald. Lancet 1: 403-404 (Feb. 21) 1959 [London].

The author shows that in the controversy about home or hospital confinement all that really matters is, "What is best for mother and child?" The mother's house has the advantages that the family circle is not disrupted, that there is less risk of cross infection, and that most homes are more comfortable than most hospitals. Disadvantages are that in case of any unforeseen complications (e. g., postpartum hemorrhage, asphyxia of the baby) the home is not the best place for treatment. Similarly the hospital has these contrasting features: if there is any serious complication, the hospital is safer, and it may be a place of greater comfort and convenience for the actual labor. The disadvantages are that there is a much increased risk of cross infection, particularly of the baby, and, after delivery, the hospital is less comfortable than the home. The general practitioner maternity home occupies an intermediate position in that it is usually more "homey" than the hospital, yet possesses more safety factors than the mother's house. On the other hand, the maternity home is not so well staffed and equipped as the hospital and is less comfortable than most houses.

The author, a consultant obstetrician and gynecologist, feels that the reason that obstetric services are not ideal in Britain is partly due to the rigidity of administration and partly to the clash of interests in a tripartite service. In obstetrics, the family physician, the midwife, and the consultant should cooperate as members of a team, and the care of every pregnant woman should be the function of the team. In different circumstances a predominant share may be taken by one or other of the partners. In the region where the author practices, all pregnant women are first seen by the general practitioner. Any whom he identifies as "abnormal" are directed to the hospital. All "normal" patients are screened by the consultant at a clinic in the maternity home where routine tests are performed. In these maternity home clinics, the matron of the home meets the patients, supervises their documentation, and assists at their examination, so that she too is well acquainted with them. Thereafter the antenatal care of the patient is entirely in the hands of her own physician—unless he refers her for consultation—until the 36th week. At the 36th week, she is again seen by the consultant who has a chance to detect any complications which have developed since the initial booking (e. g., toxemia, abnormal presentations, and disproportion). She is not seen again by the consultant except at her physician's specific request. The family physician supervises her antenatal care, while the conduct of labor and delivery largely devolves on the midwife, the physician being on call.

It is in the puerperium that the hospital environment is most unfavorable; and the best place for the normal puerperium is the mother's home. Such an arrangement is practicable, provided that the artificial barrier between home and hospital midwifery is removed. The author would like to see the normal mother and baby discharged home 48 hours after delivery, and then nursed as though the district were a dispersed lying-in ward. (Recent work has shown that a high proportion of babies are not colonized by hospital bacteria until after the third day.) The nurse in charge would make her rounds by car with her pupils—accompanied by a hospital resident physician for cases under the consultant. She would also look after women who are under the charge of a family physician, working with him in their care.

Pregnancy Diagnosis by the Konsuloff Test. P. Tartaglia and P. L. Tarozzi. Arch. ostet. e ginec. 63:712-720 (Nov.-Dec.) 1958 (In Italian) [Naples].

The authors investigated the accuracy and practical application of pregnancy diagnosis by the Konsuloff test in a group of 149 pregnant women and in a control group of 30 persons, 25 of whom were nonpregnant women and 5 were men. Two milliliters of the serum or urine of these persons was injected into hypophysectomized frogs of the species, Rana esculenta. The degree of melanophoric expansion, according to the melanophore index chart given by Hogben, was read 30, 60, and 120 minutes after the injection. This series consisted of 118 women in the first trimester of pregnancy, of 12 in the second, and of 19 in the third. Positive Konsuloff reaction was obtained in 103 women pregnant in the first trimester, in 11 pregnant in the second; and in 18 pregnant in the third. Two positive reactions were also read for persons of the control group. The authors recommend pregnancy diagnosis by the Konsuloff test for the following reasons: a fairly high degree of accuracy (about 91%), speed of the test and possibility of early reading of melanophoric expansion, and the economy feature. On an average, 3 frogs were utilized to find one suitable to complete the test. The main difficulty consisted in obtaining animals in which retraction of the melanophores would have been complete. This process, in turn, seems to be related to the difficulty in performing a successful hypophysectomy.

PEDIATRICS

Perinatal Pneumonia: A Retrospective Study. F. A. Langley and J. A. McCredie Smith. J. Obst. & Gynaec. Brit. Emp. 66:12-25 (Feb.) 1959 [London].

The role of perinatal pneumonia as a cause of perinatal death is not fully understood. The authors carried out a study of pneumonia in fetuses and infants dying at St. Mary's Hospital, Manchester. The object was to determine some of the factors that contribute to such infection and to attempt an assessment of its role as a cause of perinatal death. This study is based on postmortem findings and is retrospective and thus has defects and limitations. The term "perinatal death" is employed to mean stillbirth or death in the first week of life. Pneumonia, as used in this paper, signifies the presence of polymorphonuclear leukocytes in the air spaces or interstitial tissue of the lungs in more than minimal amounts. This restriction is necessary, insofar as occasionally a few pus cells are present which have probably been aspirated at about the time of birth. The perinatal deaths for the years 1950, 1952, and 1954 were surveyed. The cases of pneumonia were arranged in groups according to the age at death, and an equal number of infants dying at the same age were taken as controls.

The authors describe observations on 87 cases of perinatal pneumonia and compare them with a control series of 85 perinatal deaths. On the basis of such factors as maturity of the infant and the parity and age of the mother, it is possible to distinguish between fetal pneumonia and late perinatal pneumonia which occurs in infants dying in the first week but after the first day. Infants dying of pneumonia on the first day of life form an intermediate group. Fetal pneumonia occurs in fetuses near full term and is commonly associated with anoxia and always with inflammation of the fetal surface of the placenta. It is difficult to decide when such pneumonia is merely aspiration of infected liquor amnii and when it is a true local inflammation. It appears likely that fetal pneumonia, or the associated anoxia, is frequently the primary terminal cause of death in such fetuses. Late perinatal pneumonia occurs in premature infants and is probably usually only a contributory or coincidental cause of death.

Staphylococcic Pneumonia in Children. O. K. Harlem. Tidsskr. norske laegefor. 79:119-124 (Feb. 1) 1959 (In Norwegian) [Oslo].

From 1950 to 1953 only 3 patients with verified cases of staphylococcic pneumonia were treated in the Children's Clinic in Bergen; from 1953 to March, 1958, 7 patients with this type of pneumonia were treated there. Only one patient was over one year of age. Two children died. The autopsy findings showed large, firm lungs containing little air and covered with thick fibrin masses, pneumonic infiltration in the tissue, and numerous abscesses filled with thick yellow pus; there was growth of yellow hemolytic coagulase-positive staphylococci. In all cases the disease started as an ordinary infection of the upper respiratory tract, with aggravation after a shorter or longer period and signs of pneumonia. It is thought likely that the way for the staphylococci is paved by a virus infection. In the course of the 4 winter months when the 7 cases of staphylococcic pneumonia occurred, 90 children with "usual pneumonia" were treated in the clinic. The average duration of confinement to bed for these children was 2 weeks; for the surviving 5 patients with staphylococcic pneumonia it was 37 days. The disease develops fast, and the closer to the first months of life the infant is, the more fulminant the course. Only rapid diagnosis and treatment can reduce the high mortality. The standard treatment was penicillin and sulfonamides in usual pneumonia doses and 30 to 50 mg. of erythromycin per kilogram daily. The erythromycin therapy must not be terminated too early—at the earliest 3 weeks after the patient is fever-free.

The author advises physicians to think of staphylococcic pneumonia when an infant has an infection of the respiratory tract and to suspect staphylococcic pneumonia when there are symptoms of pneumonia, especially if the infant is less than 6 months old and/or there are signs of extensive (possibly lobar) pneumonia (and pleural effusion). He also advises them to regard the demonstrated pneumonia as staphylococcic pneumonia if after 24 hours there is not adequate response to pneumonia treatment; the child should be hospitalized, if possible, and given erythromycin in additional treatment. A footnote mentions 4 additional cases of staphylococcic pneumonia treated later in infants under 6 months of age; 3 patients had primary and 1 had secondary staphylococcic pneumonia.

Comparative Studies on Measles and Distemper Viruses. G. Carlström. Acta pædiat. 48:25-32 (Jan.) 1959 (In English) [Uppsala, Sweden].

There have been discussions on whether the viral agent that causes distemper in dogs gives rise to infections in man. In 1953 Adams had demonstrated in human gamma globulin and human serum a substance that neutralized the virus of canine distemper. The suggestion that infection with canine distemper virus or some immunologically related agent may affect human subjects prompted the studies described in this paper.

Canine distemper virus (C.D.V.) was adapted to suckling mice, and a test was developed for the measurement of C.D.V.-neutralizing activity. The presence of C.D.V.-neutralizing substances in human subjects of various age groups was found to resemble the typical pattern of immune response to human viral infections. Evidence was obtained of a relationship between the presence of C.D.V.-neutralizing activity in human serums and past infection with measles. Furthermore, during an attack of measles the C.D.V.-neutralizing titer increased significantly from the acute to the convalescent phase.

The virus of measles (M.V.) was also adapted to suckling mice, and a test was devised for the demonstration of M.V.-neutralizing activity. M.V. and C.D.V. and corresponding antiserums were used for cross serologic titrations in baby mice. The two agents were found to be immunologically related, but an antigenic difference was demonstrable. It is suggested that measles virus, distemper virus, and rinderpest virus belong to the same group of viruses. Preliminary experiments were carried out concerning the antigenicity and pathogenicity of M.V. and C.D.V. to various species of animals, the aim being to investigate the possibility of vaccinating with C.D.V. against measles and vice versa.

Prognosis of Infantile Eczema. F. O. C. Meenan. Irish J. M. Sc. 6:79-83 (Feb.) 1959 [Dublin].

Infantile eczema usually commences as erythematous patches on the cheeks of a baby of about 3 months; these patches begin to ooze and crust over. Commonly the process spreads to the scalp and other parts of the body, and in severe cases most of the skin may become involved. The condition may clear up in a few weeks or months, or may persist with remissions and exacerbations until the child is between 18 months and 2 years. At this stage the eczematous process tends to become papular and scaly with less oozing. The irritation causes scratching, with subsequent lichenification of the skin. The usual sites for this phase of eczema are the backs of the knees, fronts of the elbow, and around the wrists. This form again can clear up within a few months or years or persist into adult life. The flexural type of infantile eczema has been referred to as "atopic dermatitis" and "Besnier's prurigo," but in this paper the flexural lichenoid eczema of childhood and early manhood is regarded as persistent infantile eczema. These patients often have a familial or hereditary background of allergic disorders. Asthma or other allergic diseases sometimes develop later in the child with infantile eczema. Present methods of treatment of infantile eczema are not very effective. The parents gradually reconcile themselves to the fact that little can be done at the time, if they can believe that the skin will eventually clear up. It is, therefore, important to know the natural history of infantile eczema.

Questionnaires were mailed to the parents of children who had been treated for infantile eczema in the Children's Hospital, Dublin, during 1932-1945. More than 50% of the parents replied. Two of the 48 children had died during infancy, one from pneumonia and the other from unspecified causes. In studying the reply to the questionnaires in 4 other cases, it was decided that a diagnosis of infantile eczema was somewhat doubtful, and they were excluded. This left 42 cases for analysis. There were 23 male and 19 female children in the series. Thirty-eight were under 2 years of age when in the hospital, and 4 were over 2. In assessing the duration of the eczema, it was possible to divide the cases into 4 groups. Group 1 included 15 children whose eczema cleared at or shortly after leaving the hospital; group 2 included 10 whose eczema cleared around the age of 8 years; group 3 included 4 whose eczema cleared between the ages of 15 and 21; and group 4 comprised 13 whose eczema has never cleared. Asthma developed in 11 of the 42 children.

OTOLARYNGOLOGY

Early Diagnosis and Treatment of Corrosive Burns of the Esophagus. E. L. Yurich. Laryngoscope 69: 131-140 (Feb.) 1959 [St. Louis].

When the author reviewed cases of corrosive burns of the esophagus reported in the literature and treated at his hospital, he observed a number of undesirable features in their management, such as (1) inadequate early diagnosis based mainly on presumptive evidence, (2) withholding of early therapy because of inadequate diagnosis, (3) institution of therapy without an accurate diagnosis, and (4) needlessly long hospital confinement. The introduction of cortisone into the treatment of esophageal burns made earlier and more accurate diagnosis more important, because it was found that cortisone was effective only in the early stages. Esophagoscopy presents a problem. Some feel that early esophagoscopy is dangerous because of the possibility of perforating a weakened esophageal wall. Others are of the opinion that esophagoscopy should be done within 24 to 48 hours of the time of the burn, while still others prefer to do it between the 4th and the 7th day after ingestion of the caustic agent.

The author presents observations on 37 patients who entered the emergency room at Receiving Hospital of the City of Detroit with symptoms and signs suggesting that a corrosive agent had been ingested. By resorting to pharyngoscopy and esophagoscopy early, he was able to identify 10 cases of actual burns among the suspected 37. Of these 10 esophageal burns, 7 were caused by sodium hydroxide, 1 by ammonia, 1 by Lysol, and 1 by an undetermined agent. The author recommends esophagoscopy within the first 24 to 48 hours. The average duration of stay in hospital for the suspected burn cases with negative esophagoscopic examinations was 2 or 3 days as compared with 2 or 3 weeks for the treated cases.

The initial treatment should neutralize the offending agent. For alkalies, acetic acid (1 to 2%) and citrus juices are given in small repeated doses; for acids, olive oil, milk, and egg whites are of value. Gastric tubes are not inserted either for lavage or for feeding purposes, as they add to the original trauma and may induce vomiting with additional corrosive effect to the esophagus. Diet begins with clear liquids, then pureed foods, and by the end of the week the patient can ordinarily tolerate semisolids. Tracheotomy and treatment for shock are carried out if required. Antibiotics are given to prevent such complications as periesophagitis, mediastinitis, pulmonary infections, abscess formation, and esophageal perforations. Other therapeutic measures include sedatives and analgesics. Steroids are given in relatively large doses, preferably within 24 hours and always within 48 hours after ingestion of the corrosive agent. The average dose for the child in the 1-to-4-year age group is 40 to 50 mg. of prednisolone daily in 4 divided doses. The duration of therapy is dependent upon the response to medication. Eight of 10 cases of esophageal burns which were treated with steroids responded favorably. A typical case is presented. Strictures developed in 2 of the 10 patients; the history of one of these is presented. Cortisone and related substances are becoming more widely accepted as an early form of therapy to reduce the likelihood or severity of stricture of the esophagus resulting from burns, but they are not the complete answer to the problem.

Traumatic Cholesteatomas of the Middle Ear. F. Escher. Acta oto-laryng. 50:47-54 (Jan.-Feb.) 1959 (In German) [Stockholm].

While the surgical treatment of post-traumatic changes within the region of the middle ear has been advocated for the prevention of endocranial complications, otologists, on the whole, have favored a conservative stand. Even today, surgical interventions after injuries to the temporal bone are not frequent, being largely limited to those on the facial nerve in post-traumatic paralysis. The author feels, however, that, in view of the recent experiences with tympanoplasty, surgical interventions will increase. This applies to those fractures in the region of the petrosa in which the fracture lines involve the tympanic cavity and the chain of auditory ossicles, and which are followed by impairment of sound conduction (longitudinal fractures of the petrous pyramid).

The author reports observations on 3 patients in whom cholesteatoma of the middle ear developed as sequel after fractures at the base of the skull. The fracture line passed through the external auditory canal, the tympanic margin, and the roof of the middle ear. It could be proved that the growth of the cholesteatoma started from the pavement epithelium near the eardrum that had been incarcerated in the fracture cleft. The author feels that the 3 case histories represent an experiment of nature proving the correctness of the theory of immigration in the genesis of cholesteatoma. In each of the 3 patients a typical cholesteatoma had developed in from 16 to 25 years after a longitudinal pyramidal fracture. Two of the patients had a true middle ear cholesteatoma, whereas the third had an auditory canal–mastoid cholesteatoma. The author mentions 2 authors who have reported similar cases; they prove that under special circumstances a traumatic stimulus of the epithelium of the auditory canal is sufficient to induce the development of cholesteatoma.

A Bacteriologically Safe Treatment in Acute Otitis Media. A. C. W. Derks and R. Voorhorst. Nederl. tijdschr. geneesk. 103:103-108 (Jan. 17) 1959 (In Dutch) [Amsterdam].

In studies on 227 ears of patients with acute otitis media not treated before, the authors observed that, when they obtained pus under sterile conditions by puncture of the tympanic membrane, Diplococcus pneumoniae, Hemophilus influenzae, and hemolytic streptococci were practically the only organisms found. Cultures on 115 pus samples of patients with relapsing otitis media, who had been treated with paracentesis and "effervescent (hydrogen peroxide) drops," yielded mostly staphylococci and other micrococci. It is assumed that these organisms were introduced into the middle ear from the outside, probably with the drops, and that they were responsible for most of the relapses and for the cases of chronic otitis media.

Three points are deemed important in the prevention of secondary infection of the tympanic cavity: (1) prevention of the introduction of staphylococci from the outside; (2) care for the proper drainage of pus; and (3) chemotherapy directed against the causal organisms. To prevent the introduction of pathogenic organisms, the authors apply 3% tincture of iodine to the external auditory canal and the tympanic membrane previous to paracentesis, i. e., the procedure is carried out under sterile conditions. Then they introduce the so-called Burow plug, a cotton plug saturated with Burow's solution (aluminum acetate). The use of Burow's plug eliminates infections of the inflamed middle ear by newly introduced bacteria and considerably shortens the period of recovery. So far no complications have been seen. The rate of relapse (more than 40% within a year with hydrogen peroxide treatment) was greatly reduced with the Burow-plug method. Only the H. influenzae infections tended to relapse in spite of the Burow-plug treatment. This may be prevented almost completely by giving a broad-spectrum antibiotic immediately after H. influenzae has been demonstrated as the causative agent. Treatment of these infections with antibiotics during a relapse did not appear to affect the proneness to further relapse.

A Critical Study of a New Ceruminolytic Agent. A. C. Reiniger, G. Bialkin, J. Q. Grant and others. A. M. A. Arch. Otolaryng. 69:293-302 (March) 1959 [Chicago].

A study of the literature revealed to the authors conflicting opinions about the different agents which have been recommended for use in the removal of cerumen, and suggested that the problem of providing a satisfactory, effective, safe ceruminolytic agent remained to be solved. It was decided to approach the problem of ceruminolysis from the viewpoint of incorporating a surface-active agent with a viscous, nonvolatile, aqueous-miscible carrier. Propylene glycol was selected as the carrier. The chemical analysis of cerumen made it evident that the surface-active agent of a ceruminolytic preparation would have to satisfy special requirements. The presence of a large quantity of protein material, which is polar in character, would have to be considered in attempting to attain the lowered interfacial tension system required for effective ceruminolysis. The surface-active agent chosen was Cerapon, a brand of triethanolamine polypeptide oleate-condensate. The problem of producing an essentially water-free mixture of a surface-active agent and propylene glycol was accomplished through special manufacturing techniques. To this virtually anhydrous, viscous mixture was added 0.5% chlorobutanol as an antibacterial preservative to insure a sterile solution and to minimize the possibility of cross infection through accidental contamination.

This new ceruminolytic agent, which is known as Cerumenex or Cerulav, was found to be nonirritating by the Draize-Woodard-Calvery rabbit eye irritation test. The local tissue responses to this drug were studied by repeated instillation into the ears of rabbits; and the responses obtained indicated an absence of any local histopathological effects. The agent exhibited a bacteriostatic and fungistatic effect when tested against Staphylococcus pyogenes var. aureus, Pseudomonas aeruginosa, and Trichophyton interdigitale. The obvious advantage of maintaining a high degree of germicidal activity in a preparation which is intended to come in contact with affected areas is satisfactorily met by this product. A preliminary screening for allergenic reactions in 20 patients indicated the absence of either allergenic or sensitizing properties in this preparation. There were no allergenic reactions observed in the subsequent clinical trial, in spite of the fact that patients with known history of allergy were included.

The ceruminolytic efficiency, studied in 230 patients, ranging in age from 3 months to 65 years, with varying degrees of cerumen accumulation, indicated a high order of activity, which produced excellent results in 204, good results in 19, and poor results in 7. The authors conclude that the new ceruminolytic agent offers a safe, efficient, and convenient means for the removal of ear wax. It is hoped that the wide use of this agent may replace the time-consuming, cumbersome, and sometimes traumatizing methods for the removal of cerumen from the external auditory canal.

THERAPEUTICS

Phenylbutazone and Experimental Neoplasia: I. Influence of Phenylbutazone on Growth and Development of Ehrlich's Adenocarcinoma in the White Mouse (Homologous Neoplastic Grafting). P. Bignardi. Arch. ital. pat. e clin. tumori 3:155-165 (Feb.) 1959 (In Italian) [Modena, Italy].

The effect of phenylbutazone on tumors was studied in 15 white male mice into which Ehrlich's adenocarcinoma had been transplanted by means of homologous grafting. The animals were divided into 2 groups. The first group, consisting of 5 mice, received the implantation of tumor but had no treatment with phenylbutazone. The second group, consisting of 10 mice, was treated for 15 days with phenylbutazone, a dose of not more than 3 mg. per day being given subcutaneously; then the tumor was implanted in these mice, and treatment with phenylbutazone was continued for an additional 5 days. These mice at the end of the treatment had received an average of 150 mg. of phenylbutazone per kilogram of body weight.

In the mice of the first group, some inflammation occurred in the dorsolumbar area on the right where the tumor had been implanted, but it disappeared within 2 days. A small reactive nodule, which tended to develop rapidly, appeared in the implanted area after 9 days, and 18 days after the implantation the neoplastic mass had become ulcerous and necrotic and showed a marked infiltrative character. In the meantime, the general condition of the animals became worse. They lost weight and refused food, and all 5 died within 31 days after the beginning of the experiment, having survived the implantation for an average of 22 days. The tumor, which was then enucleated, was found to have an average weight of 9 Gm.; it had remained latent for 9 days.

In the second group of mice which were treated with phenylbutazone both before and after the implantation, the drug had no effect on the growth of the tumor. The tumor, however, remained latent for an average period of 6 days, and the animals lived with it for an average of 17 days. The average weight of the tumor after death was similar in both groups of animals. The author believes that phenylbutazone has an inhibiting effect on the antineoplastic power of the organism. This effect is tentatively attributed to the detrimental influence that phenylbutazone is likely to have on the mesenchyma.

Prednisone and Tumors: I. Effect of Treatment with Prednisone on Growth and Development of Neoplasia Induced by Means of 20-Methylcholanthrene in the Albino Rat. L. Metri. Arch. ital. pat. e clin. tumori 3:202-213 (Feb.) 1959 (In Italian) [Modena, Italy].

The effect of prednisone on tumors was studied in 15 albino male rats in which tumor growth was induced by means of 4 subcutaneous injections of 20-methylcholanthrene, of 5 mg. each, in the dorsolumbar region. The animals were divided into 2 groups. The first group, consisting of 5 rats, received the 4 injections of 20-methylcholanthrene at intervals of 20 days but had no treatment with prednisone. The second group, consisting of 10 rats, was treated with prednisone, a dose of 1 mg. per kilogram of body weight being given 20 days before the first injection of 20-methylcholanthrene and 30 days after the fourth and last injection of this compound. In the second group the carcinogen was likewise given in a dose of 5 mg. per injection at intervals of 20 days.

The results obtained in the first group of rats can be summarized as follows: The neoplasia developed in all the animals; it remained latent for an average period of 163 days; the animals survived the neoplasm for an average period of 41 days; the average weight of the tumor after death was 37 Gm.; its histological character was that of fusocellular (or spindle-cell) sarcoma; metastasis was not found. The results obtained in the second group of rats can be summarized as follows: The neoplasia developed in all the animals; it remained latent for an average period of 198 days; the animals survived the neoplasm for an average period of 43 days; the average weight of the tumor after death was 35

Gm.; its histological character was that of fusocellular (or spindle-cell) sarcoma; no metastasis was observed.

The treatment with prednisone increased the length of latency of the induced tumor by an average of 35 days as compared with that of animals not so treated. This effect, the author believes, is caused by the mesenchymal damage and neuroendocrine imbalance resulting from hormone treatment, which, in fact, slowed down the metabolism of the pentacyclic hydrocarbon (20-methylcholanthrene) and thus weakened its carcinogenic effect.

Poisoning Due to Soporifics. S. Moeschlin. Schweiz. med. Wchnschr. 89:181-187 (Feb. 14) 1959 (In German) [Basel, Switzerland].

Deaths from barbiturate poisoning have increased in recent years. It has been estimated that 0.25% of all patients entering hospitals in Switzerland today are patients with acute poisoning due to soporifics. Of 514,546 patients who entered Swiss hospitals during 1956, 1,300 were found to have soporific poisoning; 31 of these patients died. It seems that a preference has been shown lately for using barbiturates and their derivatives to commit suicide. Concomitantly, the number of patients with chronic barbiturate addiction and intoxication is increasing too. Addiction particularly to glutethimide (Doriden), which is a nonbarbiturate and can be obtained easily without a prescription, has increased during the last 2 years. Patients who had ingested regularly 5 to 20 tablets a day over a comparatively short period of time presented irritability, emotional instability, pronounced anorexia, emaciation, sunken eyes with rings around them, twitching of the facial muscles, vertigo, headaches, and fainting spells. Detoxication in a hospital is suggested for such patients. The author thinks that steps should be taken to make such dangerous drugs more difficult to obtain.

Barbital (Veronal) and its derivatives, which are not broken down in the body and which are largely excreted by the kidneys, are the most dangerous drugs; and phenobarital (Luminal), which is excreted and broken down very slowly and which can still be detected in the urine 9 days after ingestion, is the second most dangerous drug. As small a dose as 3 Gm. of barbital may prove fatal. Drugs such as heptabarbital, hexobarbital sodium, and glutethimide and its derivatives, whose toxicity decreases in this order, are less dangerous because they are broken down and excreted rapidly. However, such drugs are fatal in large doses. Doses that are usually sublethal may prove fatal if there is sufficient alcohol in the body.

In some 60 to 70% of the patients who were admitted to the hospitals in Switzerland after the ingestion of soporifics, the intoxication was found to be mild; in 15 to 20%, moderately severe; and in 10 to 15%, severe. The treatment of choice of severe intoxication was with Megimide (beta-ethyl-beta-methylglutarimide). This is an analeptic, which counteracts the narcotic effect of the barbiturates on vital brain centers, such as those of respiration and vasomotor regulation. Excessive stimulation has to be avoided in order to prevent undesirable side-effects, such as convulsions. Megimide in a dose of 50 mg. should be given intravenously to patients with severe intoxication every 3 minutes until stretch reflexes and corneal and pharyngeal reflexes return. Administration of the drug is contraindicated for patients with mild intoxication whose reflexes and respiration are unimpaired, since it can cause convulsions. Megimide, even in large doses, does not produce a paralyzing effect, arrhythmias, or changes in the barbiturate blood levels or rate of excretion. Electrical stimulation was not as effective in the treatment of patients with severe intoxication as were Megimide and artificial respiration.

PATHOLOGY

A Comparison of Erythromycin with Oleandomycin in Combination with Other Antibiotics Against Hospital Staphylococci. H. J. Elliott and W. H. Hall. J. Lab. & Clin. Med. 53:364-375 (March) 1959 [St. Louis].

Thirty hospital strains of coagulase-positive, hemolytic Staphylococcus pyogenes var. aureus were exposed to individual antibiotics of the erythromycin group, including erythromycin, oleandomycin, oleandopen (a mixture of oleandomycin and penicillin), fortified oleandopen, and Signemycin [formerly called Sigmamycin] (a combination of 2 parts of tetracycline and 1 part of oleandomycin). These strains were then tested against pairs of all these antibiotics and bacitracin, chloramphenicol, tetracycline, penicillin, neomycin, and novobiocin. The tube dilution technique was used to measure bacteriostasis by single antibiotics, and subculture of each broth tube to an agar plate was employed to measure bactericidal end-points. The paper strip-agar diffusion method was used to test the bacteriostatic effect of antibiotic pairs. Replica plates were prepared to record the bactericidal action of antibiotic pairs.

The most active drugs as measured by bacteriostatic effect were erythromycin and Signemycin. Signemycin was more active than either of its 2 components, oleandomycin and tetracycline. The oleandomycin–penicillin mixtures were slightly more active than oleandomycin and much more active than penicillin G against these predominantly penicillin-resistant strains. Tests of the bactericidal action showed erythromycin to be the most active drug in the erythromycin group. Oleandomycin was the least active of the antibiotics tested. Cross resistance between erythromycin and oleandomycin was frequent in erythromycin-resistant staphylococci, but the reverse situation was not frequent. Additive potentiation of the bacteriostatic activity of oleandomycin and its mixtures in paired combinations with other antibiotics (agar diffusion method) appeared most frequently with bacitracin, chloramphenicol, erythromycin, and, as expected, with other oleandomycin mixtures. Potentiation of the bactericidal activity (replica plating method) was not frequent with neomycin. Tetracycline was less effective in increasing bactericidal action than in enhancing bacteriostasis.

No instances of true synergism of antibacterial effects were seen with any of the antibiotic combinations studied. Antagonism of antibiotic bacteriostasis was rare. Antagonism of bactericidal activity occurred more frequently, particularly with certain susceptible strains. One-third of the strains accounted for 82% of the instances of antagonism. Most of the antibiotic interaction, both addition and antagonism, occurred with the more susceptible strains of Staphylococcus organisms.

The Lung After Ligation of the Pulmonary Artery: Anatomicohistological and Anatomicoangiographic Investigations. E. Catena, G. D'Alfonso, G. P. Fioretti and E. Fiorelli. Arch. tisiol. 13:861-869 (Oct.) 1958 (In Italian) [Naples].

A study of anatomic, functional, and histological changes in the left lung, which was isolated from the pulmonary circulation by ligation of the proximal pulmonary artery, was carried out in 10 dogs killed from 7 to 90 days after the operation. In a dog killed shortly after the operation, the entire lung was found to be considerably contracted, the contraction being more pronounced in the upper lobe, where the incision was made, than in the lower lobe. It is possible that the thickened pleural tissue in the area where the incision was made prevented the reexpansion of the lobe. The contraction of the lung was less marked in a dog killed after a longer interval after the operation.

Angiographic findings revealed a more intense ramification of the bronchial arteries proximal to the isolated lung. The appearance of new vessels was more marked and more intense the longer the period that had elapsed between the operation and the death of the dog. The pulmonary circulation, however, was not restored. A new structure of blood vessels developed, providing direct communication between the bronchial and the pulmonary circulation. The microscopic examination of the pulmonary parenchyma in dogs killed shortly after the operation disclosed watery and gluey alveoli. Blood vessels in the alveolar regions were hardly perceptible and without blood.

The morphology of the pulmonary parenchyma had almost the normal pattern, and alveoli were normally distended in most sections of the parenchyma, particularly in those of the lower lobe in dogs killed a long time after the operation. Blood vessels in the bronchial circulation had larger calibers and thicker walls. There were no significant changes in the caliber of the blood vessels of the pulmonary circulation, except that in some there were traces of radiopaque material which had been injected into the bronchial arteries. This finding confirmed the existence of an indirect communication between the bronchial and the pulmonary arterial systems. Evidence of more direct communication between the 2 systems was found in the pulmonary parenchyma, where there were true anastomotic connections of the arteriovenous type.

Clinicopathologic Study of 33 Fatal Cases of Asian Influenza. R. Oseasohn, L. Adelson and M. Kaji. New England J. Med. 260:509-518 (March 12) 1959 [Boston].

This report deals with the clinical, epidemiologic, anatomic, and microbiological features of 33 deaths associated with Asian influenza which occurred in greater Cleveland in the autumn of 1957. Twenty-seven of the cases were studied at the Cuyahoga County Coroner's Office, and 6 were collected from 4 hospitals in the Cleveland area. Early in October several sudden and unexplained deaths in young persons were investigated by the coroner's office. Autopsies disclosed anatomic findings compatible with fatal influenza. The coroner's office then studied subsequent influenza-associated deaths. This accounts for the large proportion of cases in the series that came under investigation on a medicolegal basis. Cases were included when the following criteria were met: an influenza-like disease characterized by abrupt onset, with constitutional and respiratory symptoms frequently associated with similar illnesses in the family unit; characteristic anatomic changes in the respiratory tract; and postmortem isolation of the Asian strain of influenza virus. Eight virus-negative cases are included, in which epidemiologic, clinical, and morphologic findings were diagnostic.

The illness was characterized by acute respiratory disease in 25 patients, suggested encephalopathy in 4, and head injury in 1, and there was one sudden death 24 hours after a dental extraction under inhalation anesthesia. In 2 cases the antemortem data were inadequate to permit classification. Nineteen of the 25 respiratory deaths occurred in previously well persons. The remaining 6 had preexisting chronic cardiopulmonary disease. Twenty-eight of the 33 patients died within the first 7 days and 3 after 8 days or longer; in 2 cases the duration of illness was not known.

The anatomic abnormalities are discussed with regard to organ systems. Bilateral pulmonary congestion and edema were present in almost all the patients. Intra-alveolar hemorrhage of varying degree was noted in 29. In the majority the extent of parenchymal hemorrhage was sufficient to make the lungs dark purplish, bulky, and noncrepitant. Massive pulmonary hemorrhagic edema was a characteristic finding. Bronchopneumonia was present in 23 patients, of whom 3 had at least one lobe completely consolidated. There was 1 case of lobar pneumonia without bronchopneumonia, and 3 of interstitial pneumonia. Eleven of the patients with pneumonia had an accompanying fibrinous pleuritis, and in 7 blood-tinged pleural fluid was present. The hearts showed mostly nonspecific "toxic" changes—that is, a pale, flabby myocardium and bilateral cardiac dilatation. Subepicardial and subendocardial petechiae and hemorrhagic extravasation were seen in 6 patients. The most striking abnormalities in the brain were diffuse congestion and generalized swelling, manifested by flattening of the gyri, narrowing of the sulci, and an increase in weight. In several cases the degree of cerebral swelling was sufficient to produce a prominent cerebellar pressure cone and associated hippocampal and uncal changes. In no case were there microscopic changes indicative of encephalitis. The lymphoid tissue in almost all cases showed some type of acute change. The tracheobronchial lymph nodes were congested, succulent, and prominent ("reactive hyperplastic adenitis"). The authors also comment on the microscopic aspects of the pathological changes in some of the organs.

In general, postmortem pulmonary findings were similar to those reported in the pandemic of 1918-1920 and subsequent epidemics. Myocarditis was present in almost a third of cases. Although the hemolytic Staphylococcus was the most common bacterial pathogen recovered from the respiratory tract, bacteria-free cases were frequent. Asian-strain influenza virus was isolated from the lung or trachea of 25 of the 33 patients and, in addition, from the extrapulmonary organs in 3 of the 25. This finding lends support to the concept of viremia in overwhelming influenza infection in man.

Intracranial Adrenal Gland: A Case Report. M. F. Wiener and S. A. Dallgaard. A. M. A. Arch. Path. 67:228-233 (Feb.) 1959 [Chicago].

A 49-year-old man was in extremis, deeply comatose, and cyanotic when hospitalized. He was pronounced dead 20 minutes later. According to the history given by the wife, the illness began 6 days previously with persistent and increasingly severe headache. On the morning of admission to the hospital, while he was dressing to go to work, the headache became so severe that he returned to bed. In a short time he became unconscious and began having tonic convulsions at 2-to-3-minute intervals. As the coma deepened, the convulsions diminished. Treatment consisted of oxygen by tent and artificial respiration when respiration ceased. The clinical diagnosis was cerebral thrombosis or brain tumor.

At autopsy, the leptomeninges showed diffuse congestion and edema, with darkly mottled areas. As the brain was lifted, a pancake-shaped mass was found loosely attached to the pia-arachnoid of the lateral portion of the inferior surface of the left frontal lobe. The brain was placed in 10% formalin fixative for 10 days and then examined by serial coronal sections. The mass showed the structural pattern of an adrenal gland with fibrous capsule, cortical zonation, and medulla. The anatomic diagnosis was (1) intracranial adrenal gland and (2) massive intraventricular hemorrhage. Dissection failed to reveal any adrenals at the normal retroperitoneal sites. As far as the authors were able to ascertain, this is the first recorded instance of an intracranial adrenal gland. They suggest several possible mechanisms for the organogenesis of an intracranial adrenal gland.

Advantage of Purgation in Recovery of Intestinal Parasites or Their Eggs. A. D. Alicna and E. J. Fadell. Am. J. Clin. Path. 31:139-141 (Feb.) 1959 [Baltimore].

Specimens of feces were obtained from soldiers and their dependents, many of whom had been in Korea or who were originally from Puerto Rico, known areas of high intestinal parasitic infection. The effectiveness of the collection of feces after a purge with sodium chloride solution in demonstrating parasitic infections was compared with that after regular bowel movements. If examination had been limited to normally evacuated feces, many infections would have been missed. This is most emphasized in the instance of Endamoeba histolytica in that, continuing the comparisons for 5 days, the normally passed feces were positive in 63 instances, whereas the feces collected after the purge were positive in 72. For protozoal organisms the formalin-ether and zinc-sulfate flotation methods consistently yielded a higher percentage of positive findings compared with other concentration methods. For helminthic eggs and larvae the acid-ether method proved more effective. The direct-smear technique was frequently effective, especially for trophozoites and eggs of Schistosoma mansoni, but it was still necessary to supplement this procedure with one of the other methods. At least 3 fecal specimens should be studied after purgation to yield the highest number of positive findings. The method of using Scotch tape for larvae and eggs of Enterobius vermicularis yielded highly satisfactory results. Thus, the purged feces with direct smear, formalin-ether sedimentation, and acid-ether centrifugation seem to give the most satisfactory results. For E. vermicularis infection, the method with Scotch tape is adequate.

BOOK REVIEWS

X-Ray Diagnosis of the Alimentary Tract in Infants and Children. By Edward B. Singleton, Director of Radiology, Texas Children's and St. Luke's hospitals, Houston. Cloth. $11. Pp. 352, with 215 illustrations. Year Book Publishers, Inc., 200 E. Illinois St., Chicago 11, 1959.

Dr. Singleton has produced a book that will probably become a standard reference in its field. Starting with the esophagus and ending with the anus each part of the gastrointestinal tract is carefully described, with respect to normalcy and congenital and acquired lesions. By correlating anatomy, embryology, physiology, and history the roentgenologic diagnosis is made more meaningful. The technique of roentgenologic examination is clearly outlined for all ages so that the procedure can be duplicated without difficulty. The illustrations are plentiful, well planned, and excellent in quality. The author's style is clear and each part of the anatomy is covered in detail without burdening the reader with extraneous material. The reference lists are brief but wisely chosen. For pediatricians and radiologists this timely book should help solve many problems.

The Rorschach and the Epileptic Personality (Le test de Rorschach et la personalité épileptique). By J. Delay, P. Pichot, T. Lempérière and J. Perse. Translation by Rita and Arthur L. Benton. With introduction by Arthur L. Benton, and commentary by Zygmunt A. Piotrowski. [French edition copyrighted 1955, by Presses universitaires de France.] Cloth. $6. Pp. 265, Logos Press, Box 273, Cooper Station, New York 3, 1958.

This book, originally published in France in 1955, is now available in the United States. It presents an excellent review of 77 articles on Rorschach studies in epileptic patients. The authors have conscientiously covered all the literature available between 1921 and 1956. In a commentary at the beginning of the book Dr. Piotrowski states, "In all the vast literature on the Rorschach method there is nothing like this book. It summarizes succinctly, but without omitting numerous important details, everything, probably, that has been said on the subject of Rorschach findings in epilepsy."

Section 1 reviews the theories of the epileptic personality. In reading section 2 close contact with a psychologist may be necessary, or the reader may find himself puzzled by technical details. The four pages of conclusions of this section, beginning on page 169, are very helpful. Section 3 describes Rorschach studies performed on 50 ambulant epileptic patients. Section 4 gives detailed clinical observations on two patients. Section 5 presents an excellent summary of the authors' views. There is a fine bibliography. An addendum presents five studies, not included in the original French editions, carrying the study through 1956 and adding much to the value of the book. This book is recommended to anyone interested in a theoretical approach to the subject of the epileptic personality.

Emergency Surgery. By Hamilton Bailey, F.R.C.S., F.A.C.S., F.R.S.E. Seventh edition. Cloth. $32.50. Pp. 1197, with 1576 illustrations. Williams & Wilkins Company, 428 E. Preston St., Baltimore 2; John Wright & Sons, Ltd., 42-44, Triangle West, Bristol 8, England, 1958.

Those who have followed this book through its various editions have recognized in its intrinsic merit the monumental handwork of an experienced surgeon. Many of the chapters have been completely rewritten, and credit is given to a number of collaborators. Almost 10 years have elapsed since the last edition, and progress in surgery has been continuous during this time. Much of the emphasis in the text is placed on the view of the surgeon as a clinician. Technique is stressed, particularly the technique of diagnosis from the clinical standpoint. The modern surgical textbook has become, in some instances, a reflection of surgical pathology and surgical physiology, containing relatively little to guide the surgeon in clinical life. This book is for the practicing surgeon. The illustrations are clear. The use of the eponym, which provides no information of practical value, has become less frequent. Every practicing surgeon should have this book in his library.

Vascular Spiders and Related Lesions of the Skin. By William Bennett Bean, M.D., Professor of Medicine, Head of Department of Internal Medicine, College of Medicine, State University of Iowa, Iowa City. Cloth. $8.50. Pp. 372, with 131 illustrations. Charles C Thomas, Publisher, 301-327 E. Lawrence Ave., Springfield, Ill.; Blackwell Scientific Publications, Ltd., 24-25 Broad St., Oxford, England; Ryerson Press, 299 Queen St., W., Toronto 2B, Canada, 1958.

In this book Dr. Bean throws light on a group of vascular lesions and diseases which usually receive scant attention in medical books because they are thought to be unimportant and not the province of any one specialty. He does it in a delightful literary style, documenting his material thoroughly and recording his observations faithfully and in an interesting manner. One-third of the book is devoted to vascular spiders and palmar erythemas, with speculations and facts about the mechanisms involved. Case reports and documentary evidence are combined with thought-provoking comments, which round out this section. Excellent discussions of metastatic carcinoid, Osler's disease,

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These book reviews have been prepared by competent authorities but do not represent the opinions of any medical or other organization unless specifically so stated.

hemangiomas, and dyschondroplasia, generalized telangiectasia, strawberry marks, livedo reticularis, glomus tumor, and other cutaneous vascular lesions are also presented. What is known of the natural history of the conditions is presented, as are hypotheses about their cause.

The section on vascular spiders is so outstanding that, by comparison, the rest of the book seems to lag, but since much new material as well as that not found easily elsewhere is presented, the reader's interest is sustained. Abundant references, excellent illustrations, and numerous case histories highlight the text. The conclusions amplify the author's integrity as a reporter and observer and establish him as an articulate, provocative, and entirely readable writer. His enthusiasm, clinical acuity, and desire to relate seemingly unrelated and superficial findings permeate the book. It represents the finest type of medical writing on both the medical teaching and literary level. It should be an outstanding contribution to American medical literature and is recommended for reading by student, teacher, and practitioner.

The Anatomy of the Nervous System: Its Development and Function. By Stephen Walter Ranson, M.D., Ph.D. Revised by Sam Lillard Clark, M.D., Ph.D., Professor and Chairman of Department of Anatomy, Vanderbilt University School of Medicine, Nashville. Tenth edition. Cloth. $9.50. Pp. 622, with 434 illustrations. W. B. Saunders Company, 218 W. Washington Sq., Philadelphia 5; 7 Grape St., Shaftesbury Ave., London, W. C. 2, England, 1959.

The orientation of this 10th edition of an excellent textbook of human neuroanatomy, designed for medical and other graduate students, is primarily anatomic, but its blending of morphology and function should enhance the student's knowledge not only of how the nervous system is made up but also of its operation. The plan of organization is the same as in the ninth edition; 20 chapters are devoted to the gross and microscopic anatomy and functions of the principal subdivisions of the nervous system and one chapter to clinical illustrations. There is an atlas of brain and brain stem sections, a laboratory outline, a bibliography, and an index.

Among the important changes from the previous editions are the grouping of drawings of brain stem nuclei with the corresponding drawings of Weigert preparations, a feature of great value to the student; use of the Parisiensia Nomina Anatomica, 1955, where possible; the inclusion of six electron micrographs; and numerous modifications of the text. The illustrations are abundant and clear and the type is easy to read. The binding is sturdy and the cover durable and attractive. As in previous editions, the authors' style is straightforward and most readable. A few minor spelling errors have crept in and two figure references on pages 65 and 76 were incorrect. In general, however, the text and illustrations seem to be remarkably free of errors. This volume can be recommended with enthusiasm for medical students, graduate students in neurology and psychology, and those physicians who wish to review the anatomy of the nervous system.

The Kidney: An Outline of Normal and Abnormal Structure and Function. By H. E. de Wardener, M.B.E., M.D., F.R.C.P., Senior Lecturer in Medicine, St. Thomas' Hospital, London. Cloth. $10. Pp. 338, with 74 illustrations. Little, Brown & Company, 34 Beacon St., Boston 6; J. & A. Churchill, Ltd., 104 Gloucester Pl., Portman Sq., London, W. 1, England, 1958.

This monograph has many brief chapters on all the clinical forms of renal disease. The author is a shrewd and experienced clinician who has a lively curiosity about the structure and functions of the kidney and has contributed valuable studies on renal disease and renal function to the British medical literature. The first 90 pages deal with structure, function, functional tests, and the relation of the kidney to hypertension and edema. The book is concisely and clearly written, and it is illustrated with line drawings based on photographs. These show such things as the appearance of glomerular loops and of tubules in electron microscopic detail. The charts of functional tests cover a wide range, including the effect on the urine flow of a patient after a brief interview with a surgeon. The author emphasizes the details of laboratory testing and urine collection which are so often neglected, although it is on these details that accurate diagnosis depends. The diet lists, unfortunately, are purely British and include many proprietary products unheard of in this country. The composition of cod, however, is given in three forms (steamed, grilled, and fried in batter); beans are ignored, as are rice, corn, and potatoes. This is a book all American physicians should find useful and it is to be hoped that future printings or editions will have diet lists suited to North America, as well as a discussion of the newer diuretics, such as chlorothiazide.

The Roots of Psychoanalysis and Psychotherapy: A Search for Principles of General Psychotherapeutics. By S. A. Szurek, M.D., Professor, Department of Psychiatry, University of California School of Medicine, San Francisco. Cloth. $4.25. Pp. 134. Charles C Thomas, Publisher, 301-327 E. Lawrence Ave., Springfield, Ill.; Blackwell Scientific Publications, Ltd., 24-25 Broad St., Oxford, England; Ryerson Press, 299 Queen St., W., Toronto 2B, Canada, 1958.

The author is a psychoanalyst experienced in the treatment of children as well as adults. In part 1 he discusses a number of variables that are important to consider with reference to psychoanalysis and other forms of psychotherapy, such as the nature or severity of the patient's disorder, the skill of the therapist, the frequency of sessions, the total duration of therapy, and certain general aspects of the analytic or therapeutic situation. Part 2 is a concise, vivid, clinically descriptive account of what the psychoanalyst does for and with his patient and how he does it. Part 3 traces the basic elements of these therapeutic processes in other forms of psychotherapy, in particular those with a psychoanalytic orientation. These chapters provide valuable technical hints for the experienced psychotherapist, such as suggestions how to help the patient overcome silences, blank periods, and blocks, and how to help him verbalize material that dares break through the repressions only in the form of bodily motions and gestures.

This book is written in an engaging, easily readable style, in simple effective language, with admirable avoidance of all but the most necessary special technical terminology. Its emphasis on fundamentals and their practical application as well as its concreteness and brevity recommend it as a manual for the student, including the postgraduate student, to be used in conjunction with teaching or training courses. It can also be recommended to the general physician who is interested in the treatment of emotional and mental disorders or wants concrete information as to how the psychiatrist, psychotherapist, or psychoanalyst works and what they can do for the patients he may refer to them. The book offers an admirable description of technique, goals of treatment, and therapeutic interaction between patient and physician. The clinical scientist, however, will miss a more precise determination of indications beyond a general implication that not all patients are analyzable, and a discussion of results, successes as well as failures, with reference to the techniques used.

Therapeutic Radiology: Rationale, Technique, Results. By William T. Moss, M.D., Assistant Professor of Radiology, Northwestern University School of Medicine, Chicago. With foreword by Lauren V. Ackerman, M.D. Cloth. $12.50. Pp. 403, with 146 illustrations. C. V. Mosby Company, 3207 Washington Blvd., St. Louis 3; Henry Kimpton, 134 Great Portland St., London, W. 1, England, 1959.

This book presents an organized and rational approach to the problems of clinical radiation therapy. The various problems of treatment are well organized into chapters, augmented by a short discussion of physics, techniques, and radiobiology, and adequately illustrated by pictures and graphs. The author discusses both the curative treatment of various tumors and the palliative radiation therapy of malignancies. The treatment of benign conditions is outlined but deemphasized. There is a good discussion of treatment methods, including an outline of techniques suitable for use with conventional therapy and supervoltage equipment. Radiologists may find it a good reference work, but some of the more unusual techniques are not mentioned. This book should be of special value to cancer specialists, otolaryngologists, and gynecologists, as well as being an excellent reference for many other physicians. It is well documented by an adequate reference list at the end of each chapter.

A Short Practice of Surgery. By Hamilton Bailey, F.R.C.S., F.A.C.S., F.I.C.S., and McNeill Love, M.S., F.R.C.S., F.A.C.S. With chapters by John Charnley, F.R.C.S., William P. Cleland, M.R.C.P., F.R.C.S., and Geoffrey Knight, F.R.C.S. Eleventh edition. Cloth. 84 shillings. Pp. 1389, with 1697 illustrations. H. K. Lewis & Co., Ltd., P. O. Box 66, 136 Gower St., London, W. C. 1, England; [J. B. Lippincott Company, E. Washington Sq., Philadelphia 5], 1959.

When each new edition of an accepted work shows continued growth, as this has done, it indicates the need for such a pithy and practical book. Drs. Bailey and Love are to be congratulated on this excellent presentation. They have kept in step with the march of surgical progress. For example, those chapters dealing with the thyroid, other ductless glands, the liver, and the stomach have been rewritten completely. There is a new chapter on fluid and electrolyte balance and one on radiotherapy. The chapter on electrolytic balance is especially good. The illustrations beautifully enhance the easily readable text. This book can be recommended unreservedly to students, interns, residents, surgeons, and nurses interested in the practice of surgery.

Privileged Communications Between Physician and Patient. By Clinton DeWitt, Professor of Law, Western Reserve University, Cleveland. Cloth. $11.50. Pp. 528. Charles C Thomas, Publisher, 301-327 E. Lawrence Ave., Springfield, Ill.; Blackwell Scientific Publications, Ltd., 24-25 Broad St., Oxford, England; Ryerson Press, 299 Queen St., W., Toronto 2B, Canada, 1958.

A professor of law has written this book as the outgrowth of 30 years of experience in trial and appellate courts. He believes that members of the bench and bar have too often misunderstood the purpose of testimonial privilege. If his opinion is correct, and there is little reason to doubt it after reading the text, it must also be true that physicians do not fully understand or appreciate the nature, purpose, and extent of testimonial privilege. This book, the only one dealing exclusively with testimonial privilege, is bound to fill a long-recognized void. It contains discussions of the common-law doctrine of testimonial privilege applicable to particular confidential relationships, the physician-patient privilege statutes, the policy of the privilege, and the nature of the privilege. Two interesting and helpful chapters contain discussions of the relationship of physician and patient and the medical persons protected by the privilege. An appendix quotes statutes that are in effect in the several states regarding privilege. So technical a work as this does not have general appeal, nor appeal to or use for the busy practitioner of medicine. Medical societies might consider it as a reference work or call it to the attention of their attorneys. No physician need hesitate recommending it to a member of the bar as a useful reference work on an important and complex subject.

QUESTIONS AND ANSWERS

PERSISTENT SALMONELLOSIS

To the Editor:—*In June, 1958, because of persistent diarrhea in a newborn infant, a culture was taken and Salmonella infantis was isolated. Cultures from both parents also demonstrated this organism. A contaminated cistern was found and disinfected. Both parents were given a 10-day course of chloramphenicol therapy, and stools were cleared of this organism. The child's diarrhea was cleared with a 10-day course of chloramphenicol therapy, but stool cultures have remained positive. Two additional 10-day courses of phenoxymethyl penicillin therapy were given, but cultures have remained positive. The child is asymptomatic and has had a normal weight gain. Should further drug therapy be attempted?*

Robert Forrest Brennen, M.D., Fullerton, Pa.

Answer.—If cultures have been made of the infecting organism it would be advisable to obtain sensitivity tests for several antibiotics. Possibly it may be disclosed that chloramphenicol is not the most effective drug for the purpose desired. In the meantime it may be well to try erythromycin.

IRRADIATION OF LYMPHOID TISSUE

To the Editor:—*What is the present status of x-ray therapy to lymphoid tissue, located in and around the eustachian tube, which cannot be removed by operation?* *M.D., Ohio.*

Answer.—Lymphoid tissue is radiosensitive, and hypertrophic lymphoid tissue readily responds to irradiation and may shrink markedly, depending on the amount of irradiation administered. Where excessive overgrowth of such tissue impinges on the eustachian tube and is a factor in subsequent deafness, irradiation with x-rays is applicable and in most instances effective. A favorable response is observed in most such patients given this treatment, and there has been a definite improvement in associated deafness in many instances. When properly given by a competent radiologist, no unwarranted side-effects occur. There have been some newspaper reports concerning possible carcinogenic effects of irradiation in the throat area, but there is no specific medical evidence that cancer has developed as a result.

BLOOD HISTAMINE LEVEL

To the Editor:—*What is the best method for determining the blood histamine level? The procedure should be sufficiently accurate for clinical purposes and easy to perform, preferably with a colorimeter.* *M.D., Italy.*

Answer.—The best and perhaps the only practical method of determining the level of histamine in the blood is by a physiological assay method. The substrate is a strip of the lower part of the ileum from a guinea pig. Its reaction to the unknown is compared with the reaction with use of known standards of histamine. Several chemical methods have been reported, but none has gained favor, as they are involved and difficult and their accuracy is doubtful. Some of these have been little more than qualitative tests. The assay method requires special equipment, training, and experience.

SPONTANEOUS REMISSION OF GOITER

To the Editor:—*A 45-year-old woman was treated from her teens until she was 25 for exophthalmic goiter. Her description of nervousness, a mass in the neck, and exophthalmia seem consistent with this diagnosis. She was hospitalized and was being prepared for thyroidectomy but left the hospital without the operation being performed because of fear. Subsequently she went to the Ortman Clinic in South Dakota, where she was given treatment consisting, apparently, only of massage to the neck and to the back. She is not sure what sort of physicians treated her, but she says they called themselves bone and nerve specialists. After their treatment, her goiter and symptoms disappeared and the physicians that previously diagnosed her condition as exophthalmic goiter admitted that she had no residual signs of this disease. Assuming that the original diagnosis was correct, how can her recovery be explained? Is there any evidence that strong suggestion could cause regression of an exophthalmic goiter? Does such a condition ever regress spontaneously in adults?*

Frank C. Leitnaker, M.D.
Security Village, Colo.

Answer.—The best explanation for the course of events in this case is that the patient underwent a spontaneous remission of her symptoms of hyperthyroidism. The natural course of this disease is often characterized by periods of exacerbation and

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The answers here published have been prepared by competent authorities. They do not, however, represent the opinions of any medical or other organization unless specifically so stated in the reply. Anonymous communications cannot be answered. Every letter must contain the writer's name and address, but these will be omitted on request.

amelioration. In spite of these fluctuations, most patients show progression of their illness unless they receive definitive therapy, such as radioactive iodine, subtotal thyroidectomy, or antithyroid drugs, but spontaneous remissions with disappearance of all symptoms have been noted in rare instances.

EXAMINATION OF REMOVED LENSES

To THE EDITOR:—*The tissue committee of a hospital has asked that all cataracts be sent to the laboratory for proof of specimen removed. It is felt that the removal of a cataract can be easily ascertained postoperatively and this is a superfluous examination. Needless to say, no pathology of the lens is ever seen. Should such a procedure be required?*

Norman S. Jaffe, M.D., Miami Beach, Fla.

ANSWER.—The purpose of the histological examination of an optic lens removed because of a cataract is to establish whether the lens capsule has been included in the extraction. This is important to the surgeon for evaluation of present or future conditions that may develop in the eye. The microscopic examination of an extracted lens also has value in cases where the surgeon's statement of removal may be challenged in court procedures.

SJÖGREN'S DISEASE

To THE EDITOR:—*A 54-year-old woman has had moderately severe rheumatoid arthritis for four years. Her symptoms are controlled by 15 mg. of cortisone daily, but she has a dry mouth. The small amount of saliva present is so thick that it sticks to her mouth. What treatment would relieve this symptom?*

Everett Van Reken, M.D., Oak Park, Ill.

ANSWER.—The patient has Sjögren's disease, which is marked by dryness of all mucous membranes, resulting from a deficiency of secretion of the glands, particularly the lacrimal and salivary glands, the sweat glands, and the glands of the stomach. It occurs chiefly in women over 40 years of age. The cause is unknown. Joint changes of the rheumatoid type occur in a high percentage of patients. There is no satisfactory treatment for this condition.

STERILIZING BRUSHES

To THE EDITOR:—*How can one sterilize barbers' hair brushes, shaving brushes, and neck dusters and the brushes used by hairdressers for women?*

T. R. Pratt, M.D., Pismo Beach, Calif.

ANSWER.—The public health problem posed is one that receives far too little consideration or control in most localities, as well as in institutions for chronically ill and mentally ill patients and in penal institutions. Absolute sterilization of brushes is not required after they are commercially available, provided the manufacturer has presterilized the bristles obtained from animals which may have been infected with anthrax. Adequate disinfection destroys most bacteria and fungi which are associated with infections of the skin and hair in human beings. Among the disinfectants which can be used are quaternary ammonium compounds, such as benzalkonium chloride, ethyl and isopropyl alcohols (70 to 90% solution), formalin (1 to 3%), cresols, soaps with 2% concentrations of hexachlorophene, and 2% solution of aqueous iodine. Bichloride of mercury and mercuric cyanide should not be used. The commercially available agents should be used as directed by the manufacturer. Combs, brushes, blades of clippers, scissors, and similar items may be treated by submersion if the solution contains an antirust compound, such as sodium nitrite, to prevent corrosion of metals. Exposure intervals should normally extend for 15 to 20 minutes but should be increased when the instruments have been used on persons with known infections. Thorough mechanical cleansing and rinsing should precede submersion of the instrument in the disinfecting solution, and postsubmersion rinsing is required with most of the above preparations. Boiling for 10 to 15 minutes in water is also a satisfactory procedure if the materials can withstand heat. Formaldehyde gas cabinets are not efficient unless the humidity is carefully controlled, because moisture is essential to the activity of the formaldehyde. Ethylene oxide gas, combined with carbon dioxide to provide a nonexplosive mixture, is an excellent agent. Small units for use of such mixtures are available to physicians' offices for sterilization procedures. Perhaps one day they will be available to barber shops and beauty salons. Clean aprons used with individual neck bands or fresh towels reduce hazards of neck infections. Proper laundering and handling of the linens minimizes transmission of infecting organisms. Elimination of brushes and proper techniques in disinfecting other instruments, as practiced in the Army, also have merit.

DISCOMFORT FROM EATING SUGAR

To THE EDITOR:—*Why do some persons complain of discomfort after the ingestion of sugar? A patient with a fasting blood sugar level of 145 mg. per 100 ml. is the only man known of with this symptom, but a number of women near the menopause have complained that they cannot use sweetening.*

O. C. Amstutz, M.D., Irvine, Ky.

ANSWER.—Epigastric discomfort after the ingestion of sugar is usually secondary to increased gastric acidity and associated gastric hypermotility. A man with a fasting blood sugar level of 145 mg. per 100 ml. may have diabetes, but if his discomfort is epigastric it is probably due to the above mechanism. The associated increase in nervous tension and apprehension in women near the menopause may account for some intolerance to sugar due to increased gastric hyperacidity. One is always aware of the many preconceived notions about the menopausal syndrome in different areas.

TREATMENT OF MENINGITIS

To the Editor:—*A death recently occurred in this area from spinal meningitis. Local authorities said there was no special serum for this disease. On Feb. 17, 1959, on the television program "Highway Patrol," the case of a 6-month-old baby who had this highly contagious disease was presented. It was said that the only chance of survival was an injection of a special serum to be given within two hours. This injection was given to everyone who had come in contact with the baby. If there is such an injection, what is it? If not, is there any way that this subject could be clarified? The people in this area are quite upset.*

Nicholas M. Romano, M.D., Bangor, Pa.

Answer.—There is no antiserum that will prevent spinal meningitis. Once the diagnosis of meningitis has been made, the most effective method of treating the disease consists of the administration of sulfonamides or antibiotics.

ALLERGY TO DEODORANTS

To the Editor:—*A patient is allergic to deodorants containing any form of aluminum or hexachlorophene. Is there any deodorant to which this patient might not be allergic?*

George R. O'Daniel, M.D., Spartanburg, S. C.

Answer.—A sensitivity to aluminum and hexachlorophene rules out the use of most commercial deodorants. Aluminum salts are invariably used as the active ingredient in antiperspirants, and hexachlorophene is a widely used component in simple deodorants. Antiperspirants are classed as drugs; therefore, the presence of aluminum must be noted on the label. On the other hand, simple deodorants are classed as cosmetics, and there is no way of knowing the exact ingredients. Hexachlorophene is so effective as an antibacterial agent that it is likely to be found in a large proportion of such products. It is also not unusual to find it as an ingredient in antiperspirants. Inasmuch as manufacturers of hypoallergenic cosmetics specialize in the formulation of products to meet the needs of allergic patients, on request a simple deodorant can be formulated for this particular patient with an antibacterial substance other than hexachlorophene. The patient may find that sodium bicarbonate applied as a deodorant is effective.

ATOPIC ECZEMA AND VACCINATION

To the Editor:—*A 17-year-old boy has had atopic eczema practically all of his life. He plans to tour several European countries this summer, and to obtain a passport it is necessary that he have a smallpox vaccination. He had a successful vaccination at the age of 6. Two dermatologists have advised against giving him another vaccination. Should he be vaccinated? Is smallpox endemic in Europe?*

James O. Colley Jr., M.D., Troy, Ala.

Answer.—The mere fact that this boy had a successful vaccination at the age of 6 does not indicate that he may not have another successful vaccination. According to the laws of the United States, he must be vaccinated against smallpox if he is to be in Europe. While this consultant knows of no endemic areas of smallpox in Europe at present, this is still a legal requirement. As to whether his atopic dermatitis would be affected by revaccination, it may be said that if the condition has cleared and there are no active areas of dermatitis he may be vaccinated. If there are active areas, vaccination carries with it the risk of developing vaccinia in the areas of dermatitis, which is a serious disorder if it becomes widespread and generalized. Without knowing the extent of his active involvement, however, it is impossible to give specific advice.

INDURATED SCAR

To the Editor:—*In the Questions and Answers section of* The Journal, *March 7, 1959, page 1147, information was asked regarding treatment for a "hypertrophic scar" of a few months' duration on the upper lip. I believe the diagnosis of granuloma pyogenicum should be considered. If the lesion is truly a hypertrophic scar, judicious localized superficial x-ray would be helpful in flattening the lesion.*

S. J. Randall, M.D.
136 W. Monument Ave.
Dayton 2, Ohio.

The above comment was referred to the consultant who answered the original question, and his reply follows.—Ed.

To the Editor:—*Granuloma pyogenicum usually refers to a slowly developing tumor mass, presumably caused by suppurative organisms. At first, the pathology usually consists of masses of hypertrophic granulation tissue in an area of suppurative infection. After the acuteness has subsided and the pathology still persists, the tissue is seen to be a mass of dilated blood vessels in a well-organized connective tissue stroma, with or without any evidence of inflammation.*

The history presented in the case in question revealed no evidence of infection or suppuration. If such were the case, of course, the diagnosis of granuloma pyogenicum must be considered. There is no doubt about the value of x-ray therapy in scars, but this consultant believes that best results are obtained when radiotherapy is used early. The value of its use after as long as two months is dubious. There are some people who are more prone to hypertrophic scar formation than others. Such patients should have radiotherapy early and in larger dosage.

ARTHRITIS OF THE SPINE

To the Editor:—*A question appeared in* The Journal, *Oct. 11, 1958, page 843, regarding a patient with arthritis of the spine. Suggestions were requested with special regard to therapy. The consultant made a general statement that "the collagen and arthritic diseases are not easily separated into definite diagnostic categories." I believe the writer of the question supplied sufficient information to enable one to reach the conclusion that the patient is probably suffering from ankylosing (rheumatoid) spondylitis. If so, the consultant's recommendations are inadequate because of the omission of the possible use of phenylbutazone. Its effects are usually comparable and sometimes superior to those of radiation therapy in ankylosing spondylitis, but it must be used with due respect for its potential untoward effects. The value of corticosteroids in selected instances should also have been mentioned. Postural training is of importance, and emphasis should also be given to deep breathing exercises.*

David H. Neustadt, M.D.
628 Fincastle Bldg.
Louisville 2, Ky.

The above comment was referred to the consultant who answered the original question, and his reply follows.—Ed.

To the Editor:—*A complete discussion of the treatment of ankylosing spondylitis is not appropriate without knowing many details which were not included in the résumé submitted by the inquirer. He seemed most interested in the use of roentgen therapy, and certainly it is the consensus that x-ray therapy will help in some of the flare-ups of rheumatoid spondylitis. Which of the various forms of medical treatment might be appropriate would require further knowledge of the case; aspirin, phenylbutazone, and cortisone-like steroids would all be considered in selected cases. Physiotherapy was recommended as an inclusive program in which deep breathing and exercises would be naturally included.*

PREGNANCY AND TUBERCULOSIS

To the Editor:—*In* The Journal, *Jan. 10, 1959, page 201, inquiry was made concerning risks or complications that might be anticipated in a pregnant woman with a history of tuberculous salpingitis. Recently, several reports have appeared relative to the occurrence of ectopic pregnancy after treatment of pelvic tuberculosis Shapiro,* Obst. & Gynec. **12**:*148, 1958; Halbrecht, ibid.* **10**:*73, 1957). Halbrecht states, "Despite the growing number of cases in which tubal gestation is found to coexist with the endosalpingitis, this combination is correctly considered as rare. The role which healed tuberculosis is playing in the pathogenesis of tubal pregnancy has, on the other hand, been minimized or is not even mentioned."*

George X. Trimble, M.D.
1401 Chestnut Ave.
Long Beach 13, Calif.

The above comment was referred to the consultant who answered the original question, and his reply follows.—Ed.

To the Editor:—*There are proved cases of intrauterine pregnancy after treatment with streptomycin, aminosalicylic acid, and isoniazid. Some of the pregnancies went to term and others ended in abortion. Extrauterine pregnancy in the presence of genital tuberculosis is not as rare as intrauterine pregnancy. Occasionally the diagnosis of tuberculous salpingitis is not made in a patient with ectopic pregnancy until the pathologist's study is completed. If diagnosis of tuberculous salpingitis is made during removal of an ectopic pregnancy, the contralateral tube should be removed. If diagnosis is made later, the patient should be treated with antimicrobial agents and removal of the remaining tube. When and if antimicrobial agents are available that will definitely cure all tuberculosis, removal of the remaining tube may not be necessary.*

Extrauterine pregnancy does occur in both treated and untreated patients because the infection is bilateral and because there is marked distortion of the tubal wall and lumen. This distortion increases the chances of the occurrence of ectopic pregnancy, for the impregnated ovum becomes trapped during its descent towards the uterine cavity. In spite of the possibilities of ectopic pregnancy occurring in both treated and untreated patients with tuberculous salpingitis, some women with the knowledge of what may happen are willing to take the risk. Treatment of the salpingitis should be at least one year or even two years before pregnancy is attempted. Recurrent salpingitis has been discovered after shorter periods of treatment.

WASHINGTON NEWS

Hearings Slated on Forand Bill . .
Housing Measure Clears Congress . .
Senate Approves Big Increase in NIH Funds . .
Keogh Bill Draws Support . .
Senators Review Problems of Aging . .

FORAND MEASURE HEARINGS SCHEDULED

The House Ways and Means Committee scheduled a week of hearings this session on the controversial measure to provide health benefits to the elderly through the Social Security system. The legislation, opposed by the American Medical Association, is sponsored by Rep. Aime Forand (D., R. I.), second-ranking member of the committee headed by Rep. Wilbur Mills (D., Ark.).

Hearings were slated to begin July 13 and last for one week. The A. M. A. planned to testify in opposition to the bill that is supported by the AFL-CIO.

Despite the hearings there was no indication whether the measure would be acted upon by the influential Ways and Means Committee this session. Last year hearings also were held, but the committee did not approve the legislation.

The bill would provide, through higher Social Security taxes, hospital, surgical, and nursing-home treatment for old age and survivors' insurance beneficiaries. Cost of the program was estimated at about 2 billion dollars a year. The A. M. A. contended that the bill represents the opening wedge for socialized medicine in the United States.

CONGRESS SENDS HOUSING MEASURE TO PRESIDENT

Congress completed action on a 1.4-billion-dollar catch-all housing measure that contains provisions to encourage the construction of proprietary nursing homes. High administration officials warned that the measure might face a presidential veto because it calls for more housing spending than the administration recommended.

The nursing home provision, endorsed by the American Medical Association, authorizes loan guarantees by the Federal Housing Administration of up to 75% of a project's cost. There would be a ceiling for any one project of $12,500,000 that could be guaranteed.

State Hill-Burton authorities—those who operate the federal-state program of aid for hospital construction—would have authority to decide whether the proprietary homes had presented a case of need for the loan guarantee program. Unlike the Senate-passed version there would be no appeal to the FHA from an adverse decision by the Hill-Burton authorities.

Other features of the measure of interest to physicians would increase direct loan authorizations for interns' and nurses' housing under the college housing program from 25 million dollars to 62,500,000, and authorize a 50-million-dollar revolving fund for direct loans to help private nonprofit corporations construct rental housing for the elderly, as well as FHA mortgage guarantees for elderly persons' housing projects.

Despite the administration's opposition the bill was approved 56 to 31 in the Senate and 241 to 177 in the House, with the opposition coming mainly from southern Democrats and Republicans. The tally appeared insufficient in either house to overcome any presidential veto, an action which requires a two-thirds vote of both chambers. House and Senate Democratic leaders had agreed to trim the amount of spending originally approved by both houses in the compromise measure that was cleared by a House-Senate conference committee.

SENATE TOPS HOUSE OUTLAYS FOR MEDICAL RESEARCH

The Senate voted a sharp increase in funds for the government's main medical research arm, the National Institutes of Health. NIH would receive a total of some 481 million dollars for its activities during the fiscal year that started July 1, about 137 million dollars more than the House approved earlier this year and almost 200 million dollars more than the administration sought.

The Senate action marked the first time this session that the Senate had gone beyond the administration's recommendations in an appropriations measure. The money bill was approved by an 83 to 10 vote after a Republican economy move was buried on a 70 to 26 test vote. Over all, the measure provided $4,056,746,581 for the Department of Labor and the Health, Education, and Welfare Department and related agencies, 365 million dollars more than President Eisenhower requested.

A Senate-House conference committee is slated to work out a compromise between the measures approved by the two houses. One of the largest increases over the House level, $67,500,000, was for the Hill-Burton program of federal aid for hospital construction.

The Senate boosted to 25% the amount of research grants that may be used to pay the indirect expenses of institutions for medical research projects they are carrying on for NIH. The House-approved

(Continued on next page)

level was 15%, and the American Medical Association urged the Senate Appropriations Committee to raise this to avoid the diversions of funds "urgently needed for the medical schools teaching functions into support of research facilities sponsored by outside agencies."

WITNESSES URGE PROMPT ENACTMENT OF KEOGH BILL

More than a score of witnesses appeared before the Senate Finance Committee to advocate speedy approval of the House-passed bill providing tax deferrals for the self-employed who invest in pension plans.

Spokesmen for the American Medical Association, the American Bar Association, the American Thrift Assembly, and many other organizations of self-employed persons urged the senators to ignore administration opposition and approve the measure.

They contended it was needed in order to provide the self-employed with tax treatment similar to that now afforded salaried persons covered by company pension plans under which the company contributions are tax-exempt, and they noted that it was a matter not of avoiding taxes but of deferring payment until the self-employed person actually retires.

Rep. Eugene J. Keogh (D., N. Y.), who, along with Rep. Richard M. Simpson (R., Pa.), sponsored the legislation in the House, told the Senate committee that the discrimination in existing law should be eliminated even if it meant unbalancing the budget. He argued against putting off the effective date of the plan, as Sen. George Smathers (D., Fla.) has proposed, on grounds that the relief has been deferred already for almost a decade and that it would be doubtful if the federal budget situation ever would be favorable.

Ross L. Malone, speaking for the bar association, said that partly as a result of the present tax situation an increasing number of attorneys were leaving private practice for employment because of the security involved. This was one of the major arguments used in the case of physicians by Drs. George M. Fister and Vincent W. Archer in supporting the measure on behalf of the American Medical Association. Their testimony was reported in the previous issue of The Journal.

Dr. Roger F. Murray, representing the American Thrift Assembly, a group of organizations backing the Keogh Bill, said the Treasury Department's estimate of a 365-million-dollar annual revenue loss under the measure was "totally unrealistic." He estimated the loss during the first few years would be between 75 and 100 million dollars. Asked whether he would favor the measure if it meant unbalancing the budget, he said that he would. Furthermore, Dr. Murray testified that he would be willing to see general tax rates raised to meet the deficit.

The main opposition to the measure, in addition to the administration, which opposed it primarily on grounds of revenue loss, came from the AFL-CIO. Peter Henle of the labor group told the committee that the self-employed already have too many tax advantages. He said it was estimated that 30% of the income of self-employed persons is not reported on income tax returns. Committee Chairman Harry F. Byrd (D., Va.), closely questioned the witness on this charge, and other committee members sharply challenged the assertion.

All told, more than 70 organizations requested an opportunity to be heard on the measure, and 25 witnesses testified. Further hearings were slated for sometime in July.

PANEL SESSIONS ON AGING CONCLUDE

The first phase of the Senate investigation of problems of the elderly has been concluded. Members of the special Senate labor and public welfare subcommittee heard experts in various fields discuss in broad terms financial, psychological, medical, and other problems in the field.

Subcommittee Chairman Pat. McNamara (D., Mich.) earlier this year declared that the next step would be hearings in various cities across the country. As of this writing no schedule had been announced.

At the final day of the three-day panel session a spokesman for the Health Insurance Association of America told the subcommittee that 60% of the United States population over 65 years of age needing and wanting health insurance protection will have it by the end of this year. J. F. Follman Jr., HIAA director of information and research, testified that "as individuals, labor unions, and employers become increasingly cognizant of the importance of health insurance protection in the later years, and since the voluntary mechanism by which this protection might be provided now exists, it is reasonable to expect that the coverage of persons over age 65 in future years will increase more rapidly than has been so in the past."

Taking issue with Mr. Follman was Nelson Cruikshank, director of the AFL-CIO's department of social security, who renewed the federation's stand in favor of legislation to provide hospital and medical care to old age and survivors' insurance beneficiaries through the Social Security system. "Voluntary insurance will never be able to do it," he asserted.

Senator McNamara said he didn't know whether this was true or not, but "I hope they'll be successful."

Follman testified that some 65% of the aged needing health insurance will be covered in 1960 and about 80% of the aged will be covered by the end of 1965. "It would seem clear, then, that voluntary health insurance of quality is generally available to our senior citizens who desire such protection," he said.

Appearing before the subcommittee earlier Dr. Frederick C. Swartz, chairman of the American Medical Association's Committee on Aging, outlined the A. M. A.'s goal of "promotion of long-range positive health programs which will increase the over-all capacities of persons to live active, meaningful lives in their later years" (reported in a previous issue).

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MEETINGS

AMERICAN MEDICAL ASSOCIATION: Dr. F. J. L. Blasingame, 535 North Dearborn St., Chicago 10, Executive Vice-President.
1959 Clinical Meeting, Dallas, Texas, Dec. 1-4.
1960 Annual Meeting, Miami Beach, Fla., June 13-17.
1960 Clinical Meeting, Washington, D. C., Nov. 29-Dec. 2.
1961 Annual Meeting, New York City, June 26-30.
1961 Clinical Meeting, Denver, Nov. 28-Dec. 1.

AMERICAN

1959

July

American Society of Facial Plastic Surgery, New York City, July 17. Dr. Samuel M. Bloom, 123 E. 83rd St., New York 28, Secretary.

American Society of X-ray Technicians, Shirley Savoy Hotel, Denver, July 4-9. Miss Genevieve J. Eilert, 16 14th St., Fond du Lac, Wis., Executive Secretary.

Oregon Cancer Conference, University of Oregon Medical School, Portland, July 16-17. Dr. Martin A. Howard, 1115 S. W. Taylor St., Portland 5, Ore., Chairman.

Rocky Mountain Cancer Conference, Brown Palace Hotel, Denver, July 22-23. Dr. N. Paul Isbell, 835 Republic Bldg., Denver 2, Chairman.

August

American Congress of Physical Medicine and Rehabilitation, Hotel Leamington, Minneapolis, Aug. 30-Sept. 4. Miss Dorothea C. Augustin, 30 N. Michigan Ave., Chicago 2, Executive Secretary.

American Dietetic Association, Statler Hilton, Los Angeles, Aug. 25-28. Miss Ruth M. Yakel, 620 N. Michigan Ave., Chicago 11, Executive Secretary.

American Hospital Association, Statler Hotel, New York City, Aug. 24-27. Dr. Edwin L. Crosby, 18 E. Division St., Chicago, Director and Secretary.

American Veterinary Medical Association, Hotel Muehlebach, Kansas City, Mo., Aug. 24-28. H. E. Kingman Jr., D.V.M., 600 S. Michigan Ave., Chicago 5, Executive Secretary.

Biological Photographic Association, Inc., Sheraton-Mount Royal Hotel, Montreal, Canada, Aug. 31-Sept. 3. Miss Jane H. Waters, Box 1668, Grand Central P. O., New York 17, Executive Secretary.

National Medical Association, Detroit, Aug. 10-13. Dr. John T. Givens, 1108 Church St., Norfolk, Va., Secretary.

Nevada State Medical Association, Reno, Aug. 19-22. Dr. Gilbert G. Lenz, 505 S. Arlington Ave., Reno, Nev., Chairman.

Northwest Proctologic Society, Timberline Lodge, Mount Hood, Ore., Aug. 26-29. Dr. John L. McKay, 645 Medical Dental Bldg., Seattle 1, Secretary-Treasurer.

Rocky Mountain Radiological Society, Shirley-Savoy Hotel, Denver, Aug. 20-22. Dr. John H. Freed, 4200 E. Ninth Ave., Denver 20, Secretary-Treasurer.

Society for Clinical and Experimental Hypnosis, Fairmont Hotel, San Francisco, Aug. 3-5. Dr. Irving Schwartz, 2340 Sutter St., San Francisco 15, Chairman, Program Committee.

Southeastern Oklahoma Clinical Symposium, McAlester Clinic, McAlester, Aug. 8-9. Mr. Charles A. Miller, McAlester Clinic, McAlester, Okla., Business Manager.

West Virginia State Medical Association, The Greenbrier, White Sulphur Springs, Aug. 20-22. Mr. Charles Lively, P. O. Box 1031, Charleston 24, Executive Secretary.

September

American Association of Medical Clinics, Sheraton-Blackstone Hotel, Chicago, Sept. 24-26. Dr. Edwin P. Jordan, Box 58, Charlottesville, Va., Executive Secretary.

American Association of Obstetricians and Gynecologists, The Homestead, Hot Springs, Va., Sept. 10-12. Dr. E. Stewart Taylor, 4200 E. Ninth Ave., Denver 20, Secretary.

American Association for the Surgery of Trauma, Mount Washington Hotel, Bretton Woods, N. H., Sept. 24-26. Dr. William T. Fitts Jr., 3400 Spruce St., Philadelphia 4, Secretary.

American College of Gastroenterology, Biltmore Hotel, Los Angeles, Sept. 19-26. Mr. Daniel Weiss, 33 W. 60th St., New York 23, N. Y., Executive Director.

American College of Surgeons, The Traymore Hotel, Atlantic City, N. J., Sept. 28-Oct. 2. Dr. Paul R. Hawley, 40 E. Erie St., Chicago 11, Director.

American College of Surgeons, Ohio Chapter, Statler Hotel, Cleveland, Sept. 11-12. Dr. Berton M. Bogle, 311 S. Market, Troy, Ohio, Secretary-Treasurer.

American Roentgen Ray Society, The Netherland Hilton Hotel, Cincinnati, Sept. 22-25. Dr. C. Allen Good, Mayo Clinic, Rochester, Minn., Secretary.

American Society of Clinical Pathologists, The Palmer House, Chicago; Sept. 7-11. Mr. Claude E. Wells, 2052 N. Orleans, Chicago 14, Executive Secretary.

Central Association of Obstetricians and Gynecologists, Drake Hotel, Chicago, Sept. 24-26. Dr. Edwin J. DeCosta, 104 S. Michigan Ave., Chicago 3, Secretary.

College of American Pathologists, The Palmer House, Chicago, Sept. 6. Dr. Arthur H. Dearing, Suite 2115, Prudential Plaza, Chicago 1, Executive Director.

Colorado State Medical Society, Brown Palace and Shirley Savoy Hotels, Denver, Sept. 8-11. Mr. Harvey T. Sethman, 835 Republic Bldg., Denver 2, Executive Secretary.

International College of Surgeons, Tennessee Section, Chattanoog Sept. 28-29. Dr. William G. Stephenson, Medical Arts Bldg., Chattanooga, Tenn., Regent.

Kentucky State Medical Association, Columbia Auditorium, Louisville, Sept. 22-24. Mr. Joseph P. Sanford, 1169 Eastern Pkwy., Louisville 17, Ky., Executive Secretary.

Maryland, Medical and Chirurgical Faculty of the State of, Semiannual Meeting, Ocean City, Sept. 18. Mr. John Sargeant, 1211 Cathedral St., Baltimore 1, Executive Secretary.

Medical Progress Assembly, Tutwiler Hotel, Birmingham, Ala., Sept. 13-15. Dr. Herbert H. Thomas, 920 S. 19th St., Birmingham, Ala. Chairman, Publicity Committee.

Michigan State Medical Society, Pantlind Hotel, Grand Rapids, Sept. 28-29, Oct. 1-3. Mr. William J. Burns, 606 Townsend St., Lansing 1 Mich., Executive Secretary.

Mid-Continent Psychiatric Association, Holiday Inn Motor Hotel St. Louis County, Mo., Sept. 18-20. Dr. W. Payton Kolb, Baptist Medical Arts Bldg., Little Rock, Ark., Secretary.

Montana Medical Association, Finlen Hotel, Butte, Sept. 17-19. M L. Russell Hegland, 1236 N. 28th St., Billings, Mont., Executi Secretary.

National Recreation Congress, Morrison Hotel, Chicago, Sept. 2 Oct. 2. Mr. Jesse Reynolds, Department of Recreation and Parks, T Mosque, Laurel and Main Streets, Richmond 20, Va., Chairman.

North American Federation, International College of Surgeo Chicago, Sept. 13-17. For information write the Secretariat, 1516 La Shore Dr., Chicago 10.

Oregon State Medical Society, Medford Hotel, Medford, Sept. 23-2 Mr. Roscoe K. Miller, 1115 S. W. Taylor St., Portland 5, Ore., Executi Secretary.

Tennessee Valley Medical Assembly, Chattanooga, Tenn., Sept. 28-2 Dr. Guy M. Francis, 109 Medical Arts Bldg., Chattanooga 2, Ten Chairman.

United States Section, International College of Surgeons, Palm House, Chicago, Sept. 13-17. Dr. Ross T. McIntyre, 1516 Lake Sho Dr., Chicago 10, Executive Secretary.

Utah State Medical Association, Hotel Utah Motor Lodge, Salt La City, Sept. 16-18. Mr. Harold Bowman, 42 S. 5th East, Salt Lake City Executive Secretary.

Washington State Medical Association, Olympic Hotel, Seattle, Se 13-16. Mr. Ralph W. Neill, 1309 Seventh Ave., Seattle 1, Executi Secretary.

World Medical Association, Montreal, Canada, Sept. 7-12. Dr. Louis Bauer, 10 Columbus Circle, New York 19, Secretary-General.

October

Academy of Psychosomatic Medicine, Sheraton-Cleveland Hotel, Clev land, Oct. 15-17. For information write: Dr. Bertram B. Moss, Su 1035, 55 E. Washington St., Chicago 2, Secretary.

American Academy of Ophthalmology and Otolaryngology, T Palmer House, Chicago, Oct. 11-16. Dr. William L. Benedict, 15 Se ond St., S. W., Rochester, Minn., Executive Secretary.

American Academy of Pediatrics, The Palmer House, Chicago, O 5-8. Dr. E. H. Christopherson, 1801 Hinman Ave., Evanston, I Executive Secretary.

American Association of Medical Assistants, Benjamin Franklin Hot Philadelphia, Oct. 16-18. Mrs. Stella Thurnau, 510 N. Dearborn, Roo 924, Chicago 10, Executive Secretary.

American Association of Medical Record Librarians, Radisson Hot Minneapolis, Oct. 12-15. Miss Margaret G. Scully, 510 N. Dearborn S Chicago 10, Director.

American College of Chest Physicians, 25th Anniversary Homeco ing Meeting, Albuquerque, N. M., Oct. 14-17. Mr. Murray Kornfel 112 E. Chestnut St., Chicago 11, Executive Director.

American College of Preventive Medicine, Hotel Ambassador, A lantic City, N. J., Oct. 21-22. Dr. John J. Wright, P. O. Box 126 Chapel Hill, N. C., Secretary-Treasurer.

American Heart Association, Trade and Convention Center, Philade phia, Oct. 23-27. Mr. William F. McGlone, 44 E. 23rd St., New Yo 10, Secretary.

American Medical Writers' Association, Chase Hotel, St. Louis, O 2-3. Dr. Harold Swanberg, 510 Maine St., Quincy, Ill., Secretary.

American Otorhinologic Society for Plastic Surgery, Inc., Con Hilton Hotel, Chicago, Oct. 11. Dr. Joseph G. Gilbert, 75 Barberry La Roslyn Heights, N. Y., Secretary.

American Psychiatric Association, Detroit Divisional Meeting, Hot Statler, Detroit, Oct. 29-31. Dr. Benjamin Jeffries, 16321 Mack Av Detroit 24, Co-Chairman, Planning Committee.

American Public Health Association, Convention Hall, Atlantic Cit N. J., Oct. 19-23. Dr. Berwyn F. Mattison, 1790 Broadway, New Yo 19, N. Y., Executive Director.

American School Health Association, Claridge Hotel, Atlantic Cit N. J., Oct. 18-23. Dr. A. O. DeWeese, 515 E. Main St., Kent, Oh Executive Secretary.

American Society of Anesthesiologists, Inc., Americana Hotel, B Harbor, Fla., Oct. 5-9. Mr. John W. Andes, 188 W. Randolph St Room 1101, Chicago 1, Executive Secretary.

American Society of Facial Plastic Surgery, Chicago, Oct. 15-1 Dr. Samuel M. Bloom, 123 E. 83rd St., New York 28, Secretary.

American Society of Plastic and Reconstructive Surgery, Hot Fountainebleau, Miami Beach, Fla., Oct. 18-23. Dr. Thomas Ray Broa bent, 508 E. South Temple, Salt Lake City, General Secretary.

American Society of Tropical Medicine and Hygiene, Claypool Hot Indianapolis, Oct. 28-31. Dr. Rolla B. Hill, 3575 St. Gaudens Ro Miami 33, Fla., Executive Secretary.

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THIS WE BELIEVE

PRESIDENT'S ADDRESS

Louis M. Orr, M.D., Orlando, Fla.

IN taking office as President of the American Medical Association I do so with gratitude and humility. I am aware of the responsibilities of my new position. And I am determined to carry out my duties with all the dedication at my command. Tonight, I consider it my duty to speak out on certain fundamental ideas which are vital to medicine, to America, and to mankind.

Medical progress through the years has been inspired by a particular type of man: One who learns from the past, but faces boldly up to the future; who works at the day's task, but works and dreams, also, for tomorrow's progress.

These are the men who blaze the trail for humanity. But they must breathe the air of freedom; and they flourish best in those times and places where all men respect knowledge, value personal initiative, and applaud quality.

They have flourished in America—in this young nation which, from its beginnings, has cherished the ideals of individual freedom and self-reliance. They have flourished as the green bay tree, whether in medicine, industry, or the other professions. For it is the spirit of democracy to encourage action, cooperation, and the striving for excellence.

Disturbing Trends

Today, however, we can perceive disturbing trends in our country; and they concern all thoughtful men. In confronting these trends, we would be wise to pause for a moment and study the past, because from the past we can learn important lessons for the present.

Modern medicine, for example, traces its traditions back to Hippocrates, the Greek physician and teacher. He taught his students the facts about the art and science of medicine as they then existed. But Hippocrates gave them much more than facts; he also gave them a sense of values and ethics. He taught the physician's obligation to the patient, respect for the individual, compassion, the physician's duty to impart his knowledge to others.

Greek children were taught the meaning and value of freedom. The Greeks knew that their country was free only because they as individuals were free, and they accepted full responsibility for maintaining and protecting that freedom. They were willing to pay the price because they valued freedom above everything else. They achieved greatness not because their country was large, or rich, or blessed with abundant natural resources, for they had none of those advantages. Greece left an indelible stamp on history for one reason only: it gave birth to a spirit which for 2,500 years has sparked hope in the minds and hearts of men—the same spirit that underlies the promise of America.

When Greece and Rome eventually fell, they were conquered not by outside aggressors but by a decline in their moral and spiritual strength. Describing what happened, Miss Edith Hamilton, the famous classical scholar, has put it this way:

> In the end, more than they wanted freedom, they wanted security, a comfortable life, and they lost all—security and comfort and freedom. Is not that a challenge to us? Is it not true that into our education have come a slackness and softness? Is hard effort prominent? The world of thought can be entered in no other way. Are we not growing slack and

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Read before the 108th Annual Meeting of the American Medical Association, Atlantic City, N. J., June 9, 1959.

soft in our political life? When the Athenians finally wanted not to give to the state, but the state to give to them, when the freedom they wished most for was freedom from responsibility, then Athens ceased to be free and was never free again.

Miss Hamilton's words have a pertinent, almost ominous, ring for us Americans today. Are we teaching, living, and developing all of the potentialities of our democracy. Are we standing up for the individual over the group or the state? Are we concerned with the moral and ethical basis of our society, or do we worry more about money, and the things that money can buy? Are we exploring all possible ways and means of solving our problems through self-reliance, initiative, and cooperation, or do we more and more give up without question and accept intervention and eventual control?

The Road We Are to Travel

Let us appraise the road we are to travel.

One road leads to rigid and unworkable compulsion, to deadening uniformity, and to the loss of that individualism and vitality which have made American medicine a pacesetter in the world. This road we must not take.

The other is the road of the free spirit, of dedicated men and women voluntarily working together, of sustained and heartening progress in the never-ending war against the killers and cripplers of mankind. This is the road we have followed. This is the road we must follow. For in this way—and in this way only—can we continue to make medicine a faithful servant to mankind.

As citizens, we believe in individual freedom, individual rights, individual responsibilities. We believe that the basic element of progress is not compulsion but voluntary cooperation; not force but reason; not blind obedience but independent intelligence; not timidity but faith—faith in man, faith in ourselves, faith in God.

We believe that freedom, to survive and grow, can never be placed on a shelf and forgotten but must be fought for again and again, day after day, by men and women willing to stand up and to be counted. We reject any philosophy alien to these beliefs.

We know that we must continue to furnish the best possible health care to every American—and this emphatically includes the older citizen. We know that we must continue to improve and broaden voluntary health programs in preference to compulsory programs that lead to waste. We know that we must continue to defend the unfettered, inquiring mind, for medical progress depends on the relentless quest for truth by minds that are free.

This is not merely an opinion; it is a significant lesson of history, true yesterday, true today, true always. For the practice of medicine is more—much more—than merely facts and experience. It is new knowledge, new ideas—a blending of the best of the old with the best of the new. It is the "invincible belief" of Louis Pasteur that "science will triumph over ignorance, that the future will belong to those who have done the most for suffering humanity."

As doctors of medicine it has been our responsibility to watch men, women, and children in their darkest hours and to seek to heal and help them. Anyone who has done this knows that there is inside every man an unquenchable spirit linked to life and love, mercy and hope, and the eternal values that come from the Creator.

On this knowledge is built our firm belief—the belief that the fundamental obligation of our profession is to maintain medicine's role as the faithful servant of mankind. Now, and for always—this we believe.

DISSEMINATION OF PATHOGENIC ORGANISM BY AIR-COOLING APPARATUS.—A request was received to check an air-cooling plant installed in an operating theatre. No cases of sepsis had been recorded, but the proximity of the air stream to an operating table had given rise to concern. Inspection of the machine showed it to consist of a wall installation comprised of a rotating drum covered with porous material, which, at its most dependent point, dipped into a trough of water. . . . An electric fan sucked outside air through the drum and into the room, cooling taking place by evaporation as the drum rotated. A blood agar plate was held in the air stream, approximately 3 feet from the apparatus, and was exposed for 3 minutes. After overnight incubation, the plate yielded a profuse growth of Ps. pyocyanea. . . . Direct plating of the water yielded a heavy growth of Ps. pyocyanea. Steps were taken to clean out the water trough and to replace the contents with a solution of chlorhexidine, 1:2000 in sterile water. The solution was also poured over the drum, so as to impregnate thoroughly the porous material, after which the apparatus was allowed to remain undisturbed overnight. Subsequent water samples and air samples were proved to be free from the contaminating organism. It was recommended that chlorhexidine be periodically added to the trough, and samples submitted for bacteriological examination to exclude the presence of pathogenic microorganisms.—K. Anderson, Pseudomonas Pyocyanea Disseminated from an Air-Cooling Apparatus, *The Medical Journal of Australia*, April 18, 1959.

IS A FLUOROSCOPE USEFUL TO THE GENERAL PRACTITIONER?

Israel E. Kirsh, M.D., Hines, Ill.

Recent concern over the amount of ionizing radiation to which the public is exposed raises the question of the safety and utility of the fluoroscope in the general practitioner's office. There is evidence that the amount of exposure during fluoroscopy varies widely, as does the output of the fluoroscopes actually found in use. The busy practitioner does not always take time for his eyes to achieve maximal dark adaptation, and optimal filtration and other safety precautions have often been neglected. Fluroscopy is most valuable in observing abnormal movements. It therefore supplements the data obtained from roentgenography, which is otherwise more precise, yields permanent records, and gives more diagnostic information in proportion to the amount of radiation involved.

In view of widespread recent interest in radiation, it is timely to ask whether it is desirable for a physician to use a fluoroscope in general medical practice. As a radiologist I use the fluoroscope together with radiography in the study of diagnostic problems. That which is being questioned here is fluoroscopy without the use of x-ray films.

It has been recognized for a long time that, mainly because of limitations of the human retina, one can see much less detail in fluoroscopy than in a good radiograph. For instance, according to Deutschberger,[1] fluoroscopic vision at best is only 13% as sharp as normal visual acuity. One can discriminate shadows over 4 mm. in diameter in the lungs but only when the brightness contrast on the fluoroscreen is 20 to 40%. If the contrast is only 10%, it is not possible to see, fluoroscopically, an object smaller than 10 mm. in diameter. Henny and Chamberlain[2] state that, when fluoroscopy of a thick abdomen is done, the smallest recognizable difference in intensity may amount to 30 to 50%.

The recently sharpened medical interest in radiation has stimulated a new look at diagnostic radiology from the point of view of its danger to health versus its usefulness. A physician who uses or recommends any x-ray procedure should be able to say that it is both safe and useful. The fluoroscope in the general practitioner's office is subject to criticism on both counts.

Radiation-Safety

Let us consider briefly the question of the radiation-safety of the fluoroscopes used in hospitals and doctors' offices. These vary a great deal in radiation output per minute, and physicians differ even more in the manner in which they use the machine and in the amount of information they derive from its use.

Bell[3] showed that his own fluoroscope, as used clinically, produced 25 to 40 r per minute on the skin of the patient. During individual examinations of the chest with the fluoroscope, the output varied from 33 to 134 r per fluoroscopic examination. The doses were higher, he stated, in gastrointestinal work. He found that 148 to 396 r were actual amounts measured in single fluoroscopic examinations of the abdomen. These findings spurred Bell to obtain a new machine, with an increased distance between the tube and the table, and after that his doses were much lower. Sonnenblick[4] recently tested 117 fluoroscopes in use in physicians' offices in Newark, N. J. The output varied from 2 to 118 r per minute, 21% of his findings being in excess of 30 r per minute.

In repeating measurements of others, I showed[5] that it was possible to reduce the output of the fluoroscopes at Hines veterans hospital by adding filters to the fluoroscopic tubes. When 3-mm. aluminum filtration was used, the final dose could be reduced to 2.8 r per minute, about one-fourth of the original amount.

A requirement of fluoroscopy is that the eyes of the examiner be dark-adapted for 10 to 15 minutes, depending on the brightness of the available light. The busy practitioner often finds it difficult to wait the requisite time after seeing the patient and, as a result, is tempted to activate the fluoroscope too soon. Thus, either he suffers the handicap of less than optimal vision or he tries to increase the illumination of the screen by raising the intensity of the x-ray beam, which would result in increased radiation to the patient.

Contrast this situation with the procedure of the roentgenologist. He plans his schedule so as to perform fluoroscopy on a number of patients consecutively and retains his ocular accommodation by applying red goggles between his cases. A radiologist supplements his fluoroscopic findings with spot-films and ordinary radiographs. This permits him to make a comparison frequently of fluoroscopic and radiographic film findings on his patients. This frequent comparison benefits him in two ways. It improves his fluoroscopic ability, and it impresses him with the size and importance of lesions shown on films, which can be missed fluoroscopically. A humbling and educational experience of this kind is unavailable to the physician who depends on his fluoroscope and who does not check his findings, whether positive or negative, by x-ray films.

Since the most frequent fluoroscopic examination done by the general practitioner is that of the chest, it should be interesting to note the amount of radia-

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tion involved. Before the application of filters, tests[5] on four fluoroscopes used at Hines hospital showed outputs of 16.7, 24.0, 5.0, and 12.0 r per minute respectively. After the addition of 3 mm. of aluminum, the last-mentioned machine only registered 2.8 r per minute. If it be asssumed that the average fluoroscopic observation of the chest takes two minutes, it would follow that the total dose received by the patient is at least 5.6 r and might be much higher. On the other hand, taking an ordinary (posteroanterior) x-ray film of the chest caused only 0.031 r, or 31 mr, to be measured on the skin of the patients.[6]

Value of Fluoroscopy

When it is remembered that many times as much information is obtainable from the radiograph as from fluoroscopy, the argument for abandoning reliance on simple fluoroscopy is strong. As stated above, this is not the same as saying that fluoroscopy is useless. It is of definite value as a supplement to radiography. It may give valuable information as to the pulsation of a mediastinal mass, the amount of motion of the diaphragm, the presence of paradoxical pulsation of part of the heart border in cardiac aneurysm, or the presence of expiratory inflation of lung in obstruction of the bronchus by foreign body or tumor, for example.

But it would be a mistake to rely on the fluoroscope to detect early tuberculosis or neoplasm in the lung. It follows that if one sees nothing abnormal in fluoroscopy of the chest, it is quite risky to tell the patient that his chest is normal. These considerations apply even more strongly to examinations of the gastrointestinal tract. In fact, experience in interpreting radiographs and carrying out fluoroscopy is most important when the stomach, duodenum, and colon are concerned. Reliance on fluoroscopy alone would be poor judgment, even if the observer had had a good deal of fluoroscopic experience. There is the further consideration that if one has no radiographic equipment, the fluoroscopy inevitably is carried on for a longer time in order to reach a decision as to diagnosis. This increases the radiation to the patient (and the physician, too).

As a result of our doctrine that the spot-films and radiographs will be decisive in making the diagnosis, our fluoroscopy in the x-ray department at Hines hospital is quite short and the radiation to the patient correspondingly low. For example, the measured dose on the skin of the patient during a gastrointestinal series on an average patient at our hospital was 13.7 r for the entire procedure (fluoroscopy, six spot-films, and five ordinary films).[5] Compare this with the high figures obtained elsewhere during fluoroscopy alone.

I am sometimes asked by residents in medicine and surgery who are about to enter private practice, "What kind of fluoroscope would you advise me to buy for my office?" The reply is, as one might expect from the foregoing, "None!" If a physician can refer his patient to a radiologist for roentgenologic examination, this is the most desirable course. Fluoroscopy alone is an inferior diagnostic tool compared to complete roentgenologic examination. In addition, a radiograph is a permanent medical record, which can be studied with deliberation, carried to an expert for consultation, and compared with earlier or later films for details of progressive change.

A point of increasing importance is the demonstrated fact that radiographic examination causes less radiation to reach the patient (and physician) than does fluoroscopy. Genetic considerations require that all physicians using ionizing radiation try to reduce radiation as much as possible, and special precautions have been devised to accomplish this end. Specialists in radiology are more likely than other physicians to use modern safety precautions in this work. New types of fluoroscopic amplifying equipment are so expensive that they are impractical for general practitioners, though they can reduce radiation considerably.

In this discussion, comments concerning general practitioners apply likewise to internists and surgeons. As a matter of fact, the use by orthopedists or surgeons of the fluoroscope in reducing fractures, which is not done any more, to my knowledge, has been especially dangerous to the physician, by exposing his hands to excessive radiation.

In short, considerations of utility and safety should lead to a decline in the use of the fluoroscope by nonradiologists. This may be spurred by public (and medical) concern about radiation, but it will be motivated also by the well-informed physician's recognition of the shortcomings of this instrument, compared with balanced radiographic study.

Conclusions

Unless one checks fluoroscopic impressions with x-ray films, diagnostic errors and oversights will probably be unduly frequent, and the physician and patient may obtain a false sense of security. The use of the fluoroscope alone by the practitioner is likely to give relatively little diagnostic information for the radiation involved.

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SEROTONIN METABOLISM IN CARCINOID SYNDROME WITH METASTATIC BRONCHIAL ADENOMA

Roland E. Schneckloth, M.D., William M. McIsaac, M.B., Ph.D.
and
Irvine H. Page, M.D., Cleveland

A patient three months after lobectomy for bronchial adenoma began to experience warm flushing of the face. After a second operation for closure of a perforated duodenal ulcer the episodes became more frequent and severe and were accompanied by vomiting and other manifestations of the carcinoid syndrome. The mean daily excretion of 5-hydroxyindoleacetic acid was found to be 77 mg., approximately 10 times the normal. The urinary excretion of serotonin metabolites was found to be unaffected by the two serotonin antagonists that were tried. Histamine given intravenously did not provoke the typical flushes, and chlorpromazine had little objective effect on their course. The most significant finding was the occurrence of a hydroxyindole, probably an oxidation product of serotonin, present in the carcinoid tissue in greater amounts than serotonin itself and excreted in the urine. Its existence may explain variations in the clinical details of the carcinoid syndrome.

The clinical manifestations of malignant carcinoid tumors and their association with release of excessive amounts of serotonin (5-hydroxytryptamine) into the circulation have been well described.[1] Although 5-hydroxyindoleacetic acid is the major metabolite of serotonin excreted into the urine, it is by no means the only one. The metabolic fate of serotonin has recently been studied in experimental animals and in subjects with carcinoids, and other metabolites, such as 5-hydroxyindoleaceturic acid and N-acetyl serotonin, as well as free serotonin, have been found.[2]

The recent recognition of patients with metastatic bronchial adenoma and an associated carcinoid syndrome[3] confirmed the suggestion of Mattingly[4] that such tumors of the so-called carcinoid type might be true carcinoids and capable on occasion of functioning by liberation of serotonin. The present study was stimulated by observations of such a patient who developed the carcinoid syndrome after lobectomy for a malignant bronchial adenoma. The patient exhibited some unusual clinical characteristics such as protracted flushes lasting several days. Patients with carcinoids with similar atypical clinical features have been reported, and they have been observed to excrete not only 5-hydroxyindoleacetic acid into the urine but also increased amounts of serotonin, histamine, and the serotonin precursor, 5-hydroxytryptophan.[5] It was thought that a study of the serotonin metabolism of our patient might reveal parallel abnormalities.

Report of a Case

A man, aged 45, was admitted to the Cleveland Clinic Hospital in October, 1956, with complaint of a slight nonproductive cough for several years. Diabetes mellitus had been diagnosed five months previously. Roentgenogram of the chest revealed a lobulated shadow in the right lower lobe. On Oct. 10, 1956, a right lower lobectomy was performed. Microscopic examination of the resected specimen showed a bronchial adenoma of the carcinoid and adenocystic type; neoplasm was also found in peribronchial and hilar lymph nodes.

Three months after lobectomy the patient noted for the first time the onset of warm flushing of the face, particularly after eating. Six months after operation, perforation of a duodenal ulcer occurred requiring closure. From that time until his readmission a year later on June 6, 1958, he noted increase in frequency of flushing involving the head and neck. These episodes were commonly accompanied by nausea, vomiting, sweating, palpitations, and mild diarrhea. Flushes occurred spontaneously but could be precipitated by the administration of insulin or provoked by unusual emotional stress, and they recurred two to three times a week, lasting initially three to four hours. However, duration of attacks gradually increased, often lasting two to three days before slowly subsiding.

Physical examination during the height of a flush revealed an intense diffuse bright red discoloration of the skin of the face, neck, and upper arms, with more mottled and patchy geographical red areas on the thorax and abdomen. There was marked periorbital swelling and edema of the face, neck, feet, and ankles. The pulse was 120 per minute and blood pressure 104/62 mm. Hg lying and 100/60

From the Research Division of The Cleveland Clinic Foundation and The Frank E. Bunts Educational Institute.

mm. Hg standing. The optic fundi and lungs were normal. The heart was not enlarged, rhythm was regular, and a loud systolic murmur was heard, especially between the left sternal border and the apex. The liver was hard, nontender, and palpable 5 cm. below the costal margin.

X-ray of the chest in June, 1958, showed the heart and lungs to be normal. Proctoscopic and x-ray examination of the entire gastrointestinal tract showed no evidence of a primary tumor. The daily urinary excretion of 5-hydroxyindoleacetic acid averaged 77 mg. per 24 hours and ranged from 51 to 107 mg. per 24 hours (normal range 2 to 9 mg. per 24 hours).

Clinical Course and Treatment.—Histamine phosphate (0.025 mg.) administered intravenously did not provoke a typical flush. The patient was given intravenously 25 to 50 mg. of diphenhydramine (Benadryl) hydrochloride during flushing attacks without effect. Chlorpromazine hydrochloride in daily oral or intramuscular doses of 100 to 200 mg. had little objective effect on flushing attacks, but the patient subjectively felt much better. There was no significant change in average daily urinary excretion of 5-hydroxyindoleacetic acid (table 1), as measured by the method of Udenfriend, Titus, and Weissbach.[6]

TABLE 1.—*Urinary Excretion of 5-Hydroxyindoleacetic Acid in Patient with Carcinoid Tumor After Oral Administration of Two Serotonin Antagonists and After Removal of Metastatic Carcinoid Tissue from Liver*

Treatment	Duration of Therapy, Days	Urinary Excretion of 5-Hydroxyindoleacetic Acid, Mg./24 Hr.	
		Daily Average	Range
Control	9	77	51-107
Chlorpromazine, 100-200 mg./day	*10*	*93*	*37-173*
UML 491*			
2-4 mg./day	11	108	36-273
4-12 mg./day	9	162	122-280
	Wk. After Surgery		
Resection metastatic hepatic nodules	1	194	145-280
	2	226	140-559
	3	140	99-194
	4	150	84-239
	5	108	68-132

* UML 491 = 1-Methyl-d lysergic acid butanolamide tartrate.

The patient was given a serotonin antagonist, 1-methyl-*d*-lysergic acid butanolamide tartrate, coded as UML 491, and said to be four times more potent than *d*-lysergic acid diethylamide in antagonizing the effect of serotonin in vivo.[7] Slow intravenous infusions of 2 to 4 mg. of UML 491 during flushing attacks were followed by equivocal results. On occasion the flush appeared to be attenuated and symptoms, in part, relieved; at other times, no significant objective or subjective change in attacks was noted.

UML 491 was given by mouth in increasing doses of 2 to 12 mg. per day. The drug had no effect on blood pressure, pulse rate, or frequency and intensity of flushes. In the doses given it did not produce the bizarre psychic effects noted with lysergic acid diethylamide[8] or bromo-lysergic acid diethylamide[9] in patients with carcinoids. The daily urinary excretion of 5-hydroxyindoleacetic acid was not significantly affected (table 1).

Flushing attacks became more severe, prolonged, and incapacitating, with marked weight loss, electrolyte imbalance, and deterioration of the patient's general condition. On Aug. 8, 1958, laparotomy was done by Dr. George Crile Jr. The liver was studded with metastatic carcinoid tissue; three large tumor deposits, weighing 60 Gm., were removed from the liver. Microscopic examination revealed morphologic characteristics similar to those noted in the pulmonary tumor removed 22 months before. The patient had a difficult postoperative course because of wound infection and marked anorexia with continued weight loss. Attacks of flushing, however, were less frequent and intense and often of shorter duration. The range of daily urinary excretion of 5-hydroxyindoleacetic acid during the postoperative period was variable, but the average excretion rate showed little change (table 1). The patient was discharged and died at home a month later on Oct. 8, 1958.

Postmortem Findings.—Autopsy was performed by Dr. J. J. Dixon at the Ashtabula (Ohio) General Hospital. The immediate cause of death was a perforated duodenal ulcer with massive peritonitis. The liver was enlarged (3.24 kg.) with the bulk of the right lobe replaced by a carcinoid tumor mass showing extensive necrosis and hemorrhage; scattered throughout the remainder of the liver were multiple areas of smaller carcinoid nodules. No argentaffin granules were found in the tumor. Examination of the lungs, bronchi, mediastinum, and gastrointestinal tract failed to reveal any primary tumor.

Biochemical Investigations

Urinary Excretion of Serotonin Metabolites.—Five pooled 24-hour specimens of urine, which contained about 150 mg. of 5-hydroxyindoleacetic acid, as assayed colorimetrically,[6] were acetone-extracted,[10] and chromatography was done[2] in two solvent systems: A, *n*-propanol saturated with ammonia and, B, *n*-butanol-acetic acid-water (4:1:5). The major metabolite disclosed was 5-hydroxyindoleacetic acid; small amounts of free serotonin and 5-hydroxyindoleaceturic acid were also present but no N-acetyl serotonin or 5-hydroxytryptophan was noted.

Metabolism of Radioactive Serotonin.—Radioactive serotonin labeled with C^{14} in the β carbon atom was used for more detailed study; 2 mg. containing 4 μc of activity in aqueous solution was intravenously administered to the patient and timed-period urine specimens collected. The serotonin was more rapidly metabolized than in normal controls (normal excretion in 4 hours, 57± 3%); 82.5% of the activity appeared in the urine within 4 hours and 100% within 48 hours. This is not surprising since platelets and tissues of this patient must already have been saturated with serotonin of endogenous origin.

The indole metabolites were acetone-extracted from the radioactive urine, and chromatography was done. The chromatograms were scanned in order that the metabolites could be quantitatively estimated (table 2). Most of the dose (71.2%) was represented by 5-hydroxyindoleacetic acid and 5-hydroxyindoleaceturic acid, the products of monoamine oxidation. Minor excretion products were free serotonin (6.9%), its glucuronide conjugate (7.5%), a hydroxyindole provisionally identified as an oxidation product (5.8%), and an unknown metabolite (8.6%).

Confirmation of these results was afforded by obtaining radioautographs of the same chromatograms. Metabolites were further characterized by their R_f values in the two solvent systems and their fluorescent spectrums after elution. Although N-acetyl serotonin is normally excreted in the urine, it was absent in this case.

Carcinoid Tissue.—The carcinoid tissue removed from the liver at operation was found to contain 0.1 mg. of serotonin per gram of wet tissue. Then 25 Gm. of tumor tissue was homogenized and the indoles extracted. Chromatography of the extract showed a small amount of serotonin and a large amount of another hydroxyindole which had chromatographic properties (R_f 0.6 and 0.45, in solvents A and B respectively) and fluorescent spectrums (activation 310 mμ and emission 360 mμ) identical with a metabolite previously reported which had been provisionally identified as an oxidation product of serotonin.[2b] Visual comparison indicated this to be present in an amount approximately 10 times that of serotonin, i. e., about 1 mg. per gram of tissue.

Comment

The rarity of the production of the carcinoid syndrome by metastatic bronchial adenomas of the carcinoid type is best explained by the infrequent occurrence of distant metastases from these tumors. It is unlikely that the tumor in our patient was primary in the liver; the marked similarity of the histological picture of the bronchial adenoma to that seen in the tumor tissue in the liver two years later was sufficient to permit the consideration that they be the same neoplasm. Furthermore, at autopsy no other site for a primary carcinoid tumor could be found in the gastrointestinal tract or elsewhere. In this case and in others previously reported,[3] the syndrome was not manifest except in the presence of hepatic metastases.

A potent serotonin antagonist, 1-methyl-*d*-lysergic acid butanolamide tartrate (UML 491), failed to control symptoms of the syndrome when given by mouth, although it may have diminished the intensity and duration of some flushing attacks when intravenously administered. The relative ineffectiveness of UML 491 and other serotonin antagonists[9] in alleviating symptoms is disappointing, but such weak blocking action might be anticipated if serotonin is already bound to available specific receptor sites. Chlorpromazine, in our experience, continues to be the only serotonin antagonist which is partially effective in symptomatic relief. Surgery was undertaken because of reports of improvement after removal of liver metastases. Only a small percentage of tumor tissue could be removed and minimal therapeutic benefit resulted except for some attenuation of flushes; rapid and progressive deterioration of the condition of our patient continued.

TABLE 2.—*R_f Values, Fluorescent Spectrums, and Amount of Serotonin Metabolites in Urine of Patient with Carcinoid Tumor After Administration of 4 μc of 5-Hydroxytryptamine βC^{14} Creatinine Sulfate*

Metabolite	R_f in Solvent* A	R_f in Solvent* B	Fluorescent Spectrums,† mμ Activation (max.)	Fluorescent Spectrums,† mμ Fluorescent (max.)	Fluorescent Spectrums,† mμ pH	Metabolite Present‡ (% of total activity of urine)
5-Hydroxyindoleacetic acid	0.15	0.80	300	355	7	71.2
5-Hydroxyindoleaceturic acid	0.23	0.84	...	...	...	
5-Hydroxytryptamine glucuronide	0.35	...	...	...	...	7.5
5-Hydroxytryptamine	0.48	0.64	295	540	2	6.9
(Oxidation product)	0.60	0.45	310	360	7	5.8
N-acetyl 5-hydroxytryptamine	0.75	0.81	310	370	7	0
Unknown metabolite	0.90	...	...	...	...	8.6

* Blue spots were obtained when sprayed with p-dimethylaminobenzaldehyde in 1.5 N HCl. Solvent systems used were A, n-propanol saturated with ammonia and, B, n-butanol-acetic acid-water (4:1:5). R_f is distance traveled by compound relative to distance traveled by solvent front.

† Fluorescent spectrums were determined with Aminco Bowman spectrophotofluorometer.

‡ Quantitative estimation by scanning radioactive chromatograms.

An increased incidence of peptic and duodenal ulcers has been noted in association with the carcinoid syndrome,[11] and perforation of a duodenal ulcer was the main factor contributing to the death of our patient. Intravenously administered serotonin usually increases intestinal tone, and the administration of the serotonin precursor, 5-hydroxytryptophan, may produce gastric mucosal erosion in the rat.[12] However, serotonin itself decreases the volume and acidity of gastric secretions when injected into experimental animals[13] and ulcers in the stomach are produced only with huge doses of serotonin.[14] It is possible that the frequent association of peptic ulcer and the carcinoid syndrome is due to the excessive release of histamine in the body secondary to hyperserotonemia rather than caused by any intrinsic ulcerogenic property of serotonin itself.

Sandler and Snow[5] have noted several patients with the carcinoid syndrome who have exhibited atypical features characterized by the urinary excretion of large amounts of serotonin and also 5-hydroxytryptophan, an absence of argentaffin granules in the carcinoid tissue, a marked increase in the urinary excretion of histamine, and persistent bright red flushes of the "histamine type" which could be relieved by antihistaminic therapy. They suggest that such patients may form a distinct clinical group in which the tumors produce mainly 5-hydroxytryptophan instead of serotonin. The clinical picture and absence of argentaffin granules in the carcinoid tissue of our patient suggested that he might also belong to such an atypical group.

However, subsequent clinical and biochemical investigations did not confirm this. No 5-hydroxytryptophan was found either in carcinoid tissue or in the urine. The urinary excretion of serotonin was small. It is true that the prolonged duration of intense red histamine-like flushes lasting for days in our patient differed from the more commonly observed paroxysmal transient flushes; in most of the other reported cases of the carcinoid syndrome associated with bronchial adenoma the patient also had flushes of long duration. Unfortunately, estimations of urinary histamine levels were not made in our patient, but administration of antihistaminic drugs caused no beneficial effect, and a challenging dose of histamine did not provoke a flush.

However, the possibility that the atypical flushes were related to the presence in the tumor of some aberrant serotonin-like compound other than serotonin itself was given some support by the results of biochemical studies. The fate of serotonin in this case differed from that observed in experimental animals [2b] and in patients with the more typical clinical features of the carcinoid syndrome.[2a] Monoamine oxidation appeared, as usual, to be the major mode of inactivation, its products accounting for 71.2% of the test dose of radioactive serotonin. Excretion of serotonin unchanged and in conjugation with glucuronic acid occurred to only a small extent as normally. The major differences were the absence of an acetyl serotonin which normally occurs to the extent of 5 to 25% of the dose and the presence of an unknown compound which had not previously been observed accounting for 8.6% of the dose.

Lembeck [15] has reported that some carcinoid tissues contain, in addition to serotonin, a second pharmacologically active substance. Our most significant finding in the present case was the occurrence of a hydroxyindole, provisionally thought to be an oxidation product of serotonin, present in the carcinoid tissue in greater amounts than serotonin itself. This same product was found to be excreted in the urine to a small extent. The exact nature and physiological significance of this compound is being further investigated to see if it plays any part in the causation of some of the atypical features occasionally found clinically.

Summary

A patient with the carcinoid syndrome associated with a malignant bronchial adenoma and liver metastases was given 1-methyl-*d*-lysergic acid butanolamide tartrate (UML 491), a potent serotonin antagonist, which was ineffective in controlling symptoms when intravenously or orally administered. Chlorpromazine appeared to give some symptomatic relief. Partial resection of hepatic metastases may have temporarily diminished severity of flushing attacks but did not significantly alter progression of the disease.

A hydroxyindole compound, most likely an oxidation product of serotonin, was found in the metastatic carcinoid tissue in larger amounts than serotonin itself; small amounts of this substance were also excreted into the urine. Production by carcinoid tumors of pharmacologically active substances, other than serotonin, may on occasion account for atypical clinical features.

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The 1-methyl-*d*-lysergic acid butanolamide tartrate (UML 491) used in this study was supplied through Dr. R. Bircher of Sandoz Pharmaceuticals, Hanover, N. J.

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COLD FOOT—POSTOPERATIVE SIGN OF SILENT MYOCARDIAL INFARCTION

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The syndrome here described was observed in a man aged 40, a woman aged 53, and a man aged 37, on the 13th, 5th, and 7th days after operation respectively. It consisted in the sudden appearance of coldness and numbness in a foot, disappearance of pulsation in the distal arteries of the leg, and other signs of arterial embolism; electrocardiograms taken at this time showed recent myocardial infarction. There had not been any preexisting cardiac or peripheral vascular disease, and the only evidence of myocardial infarction was electrocardiographic. All three patients recovered on medical treatment which included anticoagulant therapy.

The purpose of this paper is to describe a syndrome that has not been previously reported. My attention was called to this clinical picture by three cases. In each instance, there developed sudden coldness of a foot in a patient without known preexisting heart or peripheral vascular disease. This observation each time led to the discovery of a silent myocardial infarction. Intensive questioning of each patient failed to reveal any history that was indicative of heart or circulatory disease prior to operation. The patients were questioned particularly in regard to chest pain on effort or with emotion, tachycardia, exertional or paroxysmal nocturnal dyspnea, orthopnea, pedal edema, effort cough, and intermittent claudication. None of these patients had had an electrocardiogram taken before operation. In each case the diagnosis of myocardial infarction was postulated before the tracing was taken.

The presence of silent myocardial infarction can be inferred by fulfillment of the following criteria: 1. Discovery of a cold foot. The contralateral foot should be warm or warmer than the affected extremity. 2. Absence of arterial pulsation in the foot and/or in other palpable arteries proximally. In other words, the dorsalis pedis artery pulsation should be absent. It may be that the posterior tibial, popliteal, and femoral pulsation could also be absent or diminished. Verification may be obtained by performing oscillometry or arteriography. 3. Plantar ischemia of the foot on elevation. 4. Normal findings on clinical examination of the heart. In other words, the rhythm should be regular (sinus) and murmurs absent. If these simple criteria are satisfied, the diagnosis of silent myocardial infarction will almost invariably be correct. The following case histories will amply illustrate these points.

Report of Cases

Case 1.—A 40-year-old man was admitted to the hospital on June 11, 1953, because of abdominal pain and vomiting. A duodenal ulcer had been discovered five years previously. He was relatively asymptomatic until one week prior to admission, when he developed severe midepigastric pain occurring one hour after meals. He failed to obtain relief from ingestion of food or alkalis. He vomited

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frequently. There was no melena or hematemesis. He had lost 10 lb. (4.5 kg.) during the preceding month, although his appetite was good.

Physical examination and laboratory studies on admission gave entirely negative results. Because of poor response to a medical ulcer regimen, partial gastrectomy was performed on June 17, 1953. Anesthetic induction was smooth. The operation lasted from 11:45 a. m. to 1:45 p. m. The anesthetic agent was cyclopropane-oxygen mixture. He received 1,500 cc. of whole blood during the procedure.

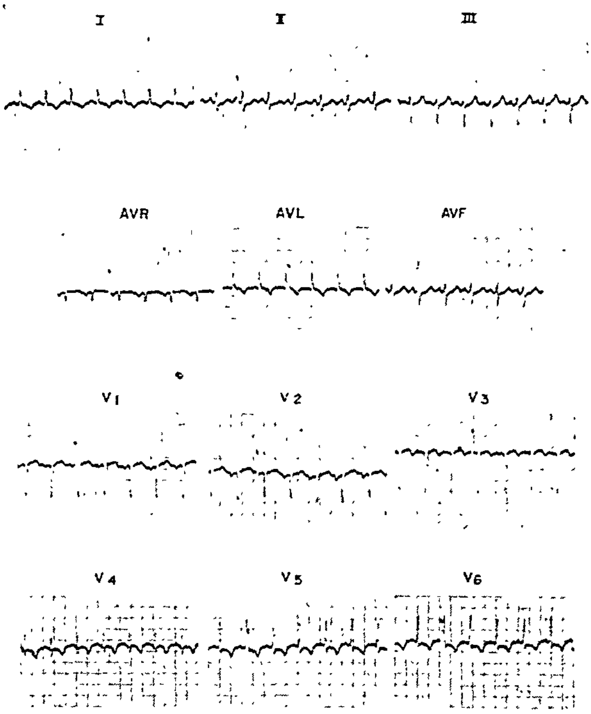

Fig. 1 (case 1).—Electrocardiogram showing recent anteroseptal infarction.

On June 30, 1953 (13 days after operation), he suddenly developed coldness of his right foot. This was associated with some pain and numbness. He was immediately given a paravertebral block at the level of L-1, L-2, and L-3 with 1 cc. of a 95% alcohol solution. No immediate effect was observed. Consultation was held about one hour after the block was given. At this time, he still complained of coldness and numbness. There was definite plantar ischemia on elevation and delayed venous filling time. The skin temperature of the foot was markedly reduced. Pulsation of the dorsalis pedis, posterior tibial, and popliteal arteries was absent. Oscillometric readings were zero to the level of the knee. The impression was arterial embolism. An electrocardiogram taken at this time (fig. 1) showed recent anteroseptal infarction.

It was decided to treat him medically rather than attempt embolectomy. On a regimen of bed rest, elevation of the head of the bed, reflex heat, analgesics, and anticoagulants, he made an uneventful recovery. He was discharged Aug. 8, 1953.

Case 2.—A 53-year-old woman was admitted for the first time on July 7, 1957, because of epigastric pain for approximately five years and tarry stools for the preceding several days. Physical examination was not revealing except for pallor and tenderness in the epigastrium on deep palpation. A hemogram showed red blood cell count 2,900,000 per cubic millimeter, hemoglobin level 9 Gm.%, and white blood cell count 5,400 per cubic millimeter, with a normal differential. A gastrointestinal series demonstrated a crater in the prepyloric region. A cholecystogram showed many calculi. Cholecystectomy was performed on July 25, 1957. She made an uneventful recovery and was discharged on Aug. 7, 1957.

She was readmitted April 8, 1958. Chills and fever had developed 10 days previously. These symptoms were associated with epigastric pain. On April 3, 1958, jaundice was noted by her family physician. There was no history of melena, acholic stools, nausea, or anorexia. A cholangiogram demonstrated numerous calculi in the common duct. A choledocholithotomy and appendectomy were done on April 14, 1958. She did well until April 19, 1958 (five days after operation), when she developed sudden coldness, numbness, and aching referring to the dorsum of the right foot. Consultation was held on

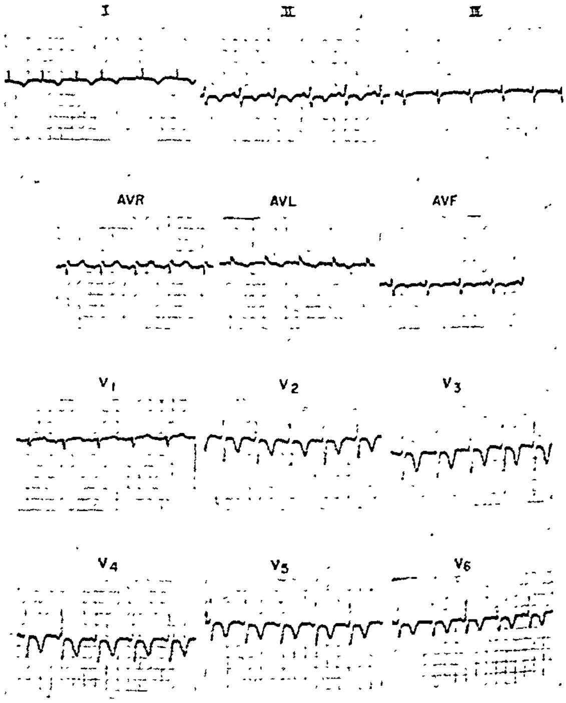

Fig. 2 (case 2).—Electrocardiogram showing recent anterior wall infarction.

April 23, 1958. The right foot was found to be cold. Plantar ischemia on elevation was 4+. An area of hyperesthesia and bluish discoloration was present over the lateral aspect of the lower third of the leg. The dorsalis pedis, posterior tibial, and popliteal pulsations were absent. Oscillometric readings were zero to the level below the knee. Examination of the heart revealed the point of maximum impulse to be in the fifth intercostal space within the midclavicular line. The rhythm was regular. No murmurs were heard. The heart sounds were of fair quality. Blood pressure was 130/80 mm. Hg. Laboratory findings prior to operation were all within normal range. An electrocardiogram (fig. 2) taken on the day of the consultation showed recent anterior wall infarction. She was placed on a medical regimen of bed rest and anticoagulants. An uneventful recovery followed.

Case 3.—A 37-year-old man was first admitted in April, 1958, for intermittent epigastric pain appearing one or two hours after meals and relieved by food and alkalis. A gastrointestinal series demonstrated a duodenal ulcer. On medical ulcer regimen, he became asymptomatic. In October, 1958, he again developed epigastric pain. The pain was constricting in nature and radiated to the back. Response to ingestion of food was variable; it was not related to effort or emotion, it would appear frequently with the patient at rest, it would last about one-half hour, and it was not associated with tachycardia. Roentgenographic studies of the gastrointestinal tract were not diagnostic. It was felt that the patient probably had a penetrating ulcer because of the persistence and severity of the pain and the failure to respond to therapy. Exploratory operation was done on Dec. 1, 1958. The period of anesthetic induction lasted one and one-half hours. Some adhesions were found in the right lower quadrant of the abdomen. The surgeon did not believe the patient's symptoms could be adequately explained by these findings. On Dec. 8, 1958 (seven days after operation), he developed severe pain in both legs. The right foot was found to be cold, pale, and paretic. No dorsalis pedis or posterior tibial pulsations could be felt. Femoral pulsations bilaterally were good. Pulses in the left leg were within normal range. He was seen in consultation Dec. 29, 1958 (29 days after operation). At this time, the right foot was still cold, pulseless, and blanched on elevation. The left leg was edematous, the superficial veins were prominent, and calf tenderness was elicited. Examination of the heart was not remarkable except for some tachycardia. It was the opinion of the consultant that the patient had had an embolus to the right leg and had developed a deep thrombophlebitis in the left leg. Oscillometry revealed zero readings to the level of the knee in the right leg and normal readings in the left leg. An electrocardiogram (fig. 3) was ordered and showed direct posterior myocardial infarction. Other laboratory findings, including blood urea nitrogen level, fasting blood sugar level, serologic tests, urinalysis, and hemograms, were normal. C-reactive protein precipitation was 4+.

He was placed on a program of bed rest and anticoagulant therapy. On Jan. 9, 1959, he developed chest pain on the right, fever, cough, and hemoptysis. Roentgenographic studies of the chest showed pulmonary infarction. The same regimen was maintained, and he was finally discharged on Feb. 12, 1959.

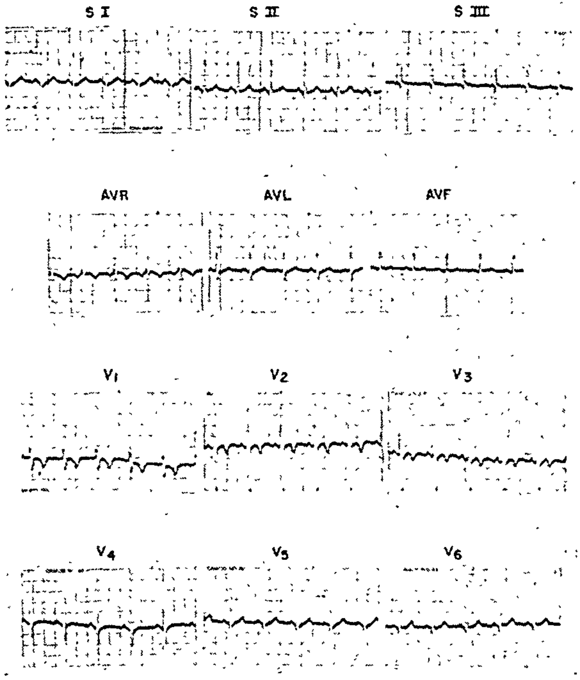

Fig. 3 (case 3).—Electrocardiogram showing direct posterior myocardial infarction.

Comment

The problem of "silent" or painless myocardial infarction has been a source of discussion and investigation for many years. Some workers feel strongly that the percentage of silent infarctions in any series is proportional to the intensiveness exercised in obtaining a history. Friedberg[1] states that the actual number of patients without pain is very small. Babey[2] could find only one patient without pain in a series of 116. Sigler[3] found pain to be absent in 4.4% of 975 patients with acute myocardial infarction and 226 with coronary insufficiency. Bean[4] reported a series of 125 patients in whom pain was noted in 75%. In a study of 70 patients with myocardial infarction without pain, Evans and Sutton[5] found that preexisting heart failure or myocardial infarction, as well as atrial fibrillation and hypertension, increased the likelihood that pain would be absent in myocardial infarction. These authors suggested that slowness of myocardial infarction rather than the size of the infarct determined the absence of pain. Pain is said to be uncommon with acute myocardial infarction occurring in Negroes, in whom dyspnea is the usual clinical manifestation. Pain may be overshadowed by other symptoms such as shock, dyspnea, dizziness, and vomiting.

In most embolisms to the extremities, the source of the embolus is the heart—usually the left side. Haimovici[6] (who has reported the largest single series) found the heart to be the source of the embolus in 96% of 330 cases. The forms of heart disease likely to give rise to intracardiac thrombi are myocardial infarction, rheumatic heart disease, acute and subacute bacterial endocarditis, and arteriosclerotic heart disease. Frequently, arterial fibrillation is present. In Warren and Linton's[7] series of 110 cases, two-thirds of the patients with fibrillation had rheumatic heart disease and one-third had arteriosclerotic heart disease. Less common causes of embolism are dislodgment of atheromatous plaques in the aorta, blood clots from thrombosed pulmonary veins, and thrombi from the systemic veins entering the left heart through a patent foramen ovale or interventricular septum and producing paradoxical embolism. To these, Gross[8] added thrombi from a closing ductus arteriosus. It is possible that emboli (made up of fragments of tumor) may invade the large arteries or, more logically, the pulmonary veins become detached and lodge in the periphery. That this actually occurs is shown in the interesting case reported by Groth,[9] in which a sarcoma of the right hip traveled to the lung as a venous embolism and from there, at a later date, became an embolism to the left femoral artery. From here, it (and its long propagating thrombus) was removed surgically, and the leg was saved. Pathological examination of the amputated right leg, a specimen of tissue from the lung, and the embolectomy specimen from the left femoral artery showed identical tumors.

After operation, a somewhat different problem is seen. I feel that the infarction occurs either during the period of anesthesia—prior to or during operation—or in the immediate postoperative period. Under these circumstances, the patient is either unaware of pain or attributes his pain to the operation. The mechanisms effecting occlusion are either hypotension, anoxia, or cardiac arrhythmias with resulting diminished cardiac output and reduced intra-aortic pressure. It was difficult to accurately determine the etiological mechanism in the above-reported cases. In the first two this was probably hypotension. In the last case, I feel that the prolonged period of anesthetic induction producing hypoxia was probably the *modus operandi.*

This syndrome is of great clinical significance because, if unrecognized, it may be instrumental in effecting a fatal outcome. One can understand that with the present trend for early ambulation of surgical patients it might be disastrous to allow such a procedure in a patient with fresh myocardial infarction. At the present time, medical and surgical personnel are keenly conscious of venous occlusive disease after operation. It would be advisable to question the patient daily not only regarding the presence of pain in the foot or calf but also whether the feet feel cold. I am convinced that some of the sudden postoperative deaths reported as being due to pulmonary embolization could well have been due to undetected myocardial infarction. It is recommended that every patient have an electrocardiogram prior to operation, so that old myocardial infarctions may be recognized. In such instances, precautions against the development of embolism might be taken. Also, an electrocardiogram should be taken after operation in the recovery room just before the patient is returned to his room.

Summary and Conclusions

"Cold foot" is a cardiovascular syndrome which is pathognomonic of silent myocardial infarction. When it occurs 4 to 21 days after operation in a patient without preexisting heart disease or peripheral vascular disease, the patient probably has myocardial infarction. Electrocardiograms should be obtained from all patients prior to and after operation.

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APPENDICITIS AFTER APPENDECTOMY

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Three patients had had appendectomy performed as a prophylactic procedure during operation for unrelated diseases. Subsequently, acute appendicitis developed in the stump left in the earlier operation. In two patients, the stump was 2 cm. in length. Appendectomy secondary to other surgery should be avoided unless the established surgical procedures of good exposure and complete appendiceal removal can be carried out.

Disease of the appendix denotes a chapter in the history of surgery which can be looked on with great pride. The manner in which the mortality has been reduced in the past half century serves as a tribute to the medical profession as a whole and reflects the benefits of many recent developments intelligently applied.[1] However, when therapeutic conquest of a certain disease is achieved, there is sometimes a tendency to forget or forego some of the established principles which led to advancement. It is then that instances begin to appear of certain poor results which are inexplicable in the light of present knowledge and therefore must be assumed to result from compromise of tested surgical principles.

Recently at the Veterans Administration Hospital, Coral Gables, Fla., we had an opportunity to see three patients with a strikingly similar disease entity. These form the basis of this report which, by accenting the above contention, may reduce the divergence from sound, time-tested methods.

Report of Cases

Case 1.—A 69-year-old man was admitted on Oct. 2, 1958, with the chief complaint of abdominal pain. The onset was 30 hours prior to admission, when lower abdominal pain developed which was crampy in character with intervening interludes of soreness. There was associated nausea and watery diarrhea but no vomiting. History revealed that the patient had multiple previous admissions to hospitals for arteriosclerotic heart disease with previous episodes of coronary occlusion and myocardial infarction. In 1950, at another hospital, a right inguinal herniorraphy was performed. The patient stated that he was told that his appendix had been removed during the course of the procedure. In April, 1958, the patient had been admitted to this hospital with complaints similar to those of his present admission. After observation and supportive therapy, remission occurred and the patient was discharged, after a transurethral resection had been performed for benign prostatic hypertrophy which was causing some obstructive difficulty.

Physical Examination.—The patient was acutely ill, appeared older than his stated age, and exhibited a marked diaphoresis. His pulse rate was 88 per minute, and his temperature was 98 F (36.7 C). The physical examination was essentially negative except for the abdominal findings, which consisted of guarding of the lower two-thirds of the abdomen, tenderness and rebound tenderness in these areas, and very occasional high-pitched peristalsis. Rectal examination revealed some tenderness anteriorly.

Laboratory studies revealed a total leukocyte count of 7,850 per cubic millimeter, with 70% neutrophils; pyuria (10 to 12 white blood cells per high-power field); and a blood urea nitrogen level of 33 mg. %. X-rays of the abdomen showed mild distention of the cecum and transverse colon with air-fluid levels in the cecum.

At operation on Oct. 3, 1958, the omentum was found to be adherent to the cecal region. Separation of the omentum from the cecum revealed an acutely phlegmonous appendiceal stump measuring 2 cm. in length and 1 cm. in diameter. Appendectomy was performed. The patient made an uneventful recovery. The pathological diagnosis was acute appendicitis with periappendicitis.

Case 2.—A 65-year-old man was admitted on Nov. 24, 1958, with the chief complaint of pain in the right lower abdominal quadrant. The present illness had begun after dinner the previous evening with sharp, stabbing pain developing in the right lower quadrant. Chills and fever, with temperature elevation up to 102 F (38.89 C), accompanied the pain. The patient consulted his family physician the morning of admission. He was given an injection for pain and advised to seek admission at this hospital.

History disclosed that the patient had been wounded by shrapnel during World War I, resulting ultimately in amputation of his right hand and arthrodesis of his right knee. In 1925, a right inguinal herniorraphy was performed during which, the patient stated, the appendix was removed. In 1935, a left inguinal herniorraphy was performed.

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Physical Examination.—The patient manifested some acute distress. His pulse rate was 72 per minute, and his temperature was 102.2 F (39 C). The remainder of the examination was negative except for the abdominal findings. There was tenderness throughout the lower abdomen, but this was more marked in the right lower quadrant and right flank region. Peristalsis was hypoactive.

Laboratory findings, including chest x-ray, abdomen films and intravenous urography, were negative except for a leukocyte count of 22,200 per cubic millimeter, with 80% neutrophils.

The patient's course in the hospital was characterized by a sudden temperature elevation to 104 F (40 C) several hours after admission. This was controlled by supportive measures, after which laparotomy was performed. At operation, an inflammatory mass consisting of an appendiceal stump about 2 cm. in length and 1 cm. in diameter was found. The stump of the appendix was surrounded by marked inflammation of the cecal wall, consisting of severe injection of the serosa, edema, induration, and friability. This inflammation, by contiguity, involved the adjacent lateral and posterior peritoneum. The end of the stump was gangrenous, and it appeared as though the tip had been sequestrated. Excision of the appendiceal remnant was not feasible because of the cecal involvement. Consequently, the region of the perforation was drained and a cecostomy performed. The patient made an uneventful recovery.

Case 3.—A 63-year-old man was admitted on Dec. 26, 1958, with the chief complaint of abdominal pain. This pain had its onset five days prior to admission, was situated mostly in the right upper quadrant of the abdomen, and was rather constant. Associated with this was anorexia and nausea but no vomiting. The patient had a normal bowel movement four days prior to admission but none since then. There was no history of jaundice.

History revealed that three years previously the patient had a partial gastrectomy for chronic duodenal ulcer disease, and he was told that the appendix was removed during this procedure. One year prior to admission he had right upper quadrant distress similar to that during this admission. This subsided spontaneously, and he was told that he had gallbladder disease.

Physical Examination.—The patient appeared acutely ill. His pulse rate was 90 per minute, and his temperature was 100.4 F (37.88 C). The physical examination was negative except for the abdominal findings, which consisted of hypoactive peristalsis, slight distention of the abdomen, and generalized tenderness which was most marked in the epigastrium and right upper quadrant.

Laboratory studies revealed a leukocyte count of 26,300 per cubic millimeter, with 93% neutrophils. X-ray of the abdomen showed distention of the small and large intestine, with separation of some of the small intestinal loops consistent with peritonitis and ileus. Fluid from paracentesis demonstrated neutrophils with gram-negative bacilli.

At operation, a generalized peritonitis was found with a tenacious exudate covering the loops of small intestine. The omentum was adherent to the cecum and was found to be confining a ruptured, inflamed appendiceal stump which projected about 0.5 cm. beyond the cecal wall. The site of perforation was drained and a cecostomy was performed. The patient's recovery was unremarkable except for a superficial wound infection.

Comment

The three case histories describe patients who had appendicitis of the appendiceal stump years after an incomplete appendectomy. These subtotal appendectomies were performed electively during operations for unrelated disease (right inguinal herniorrhaphy in two instances and gastrectomy in one).

Appendicitis of a retained stump is a recognized and documented[2] disease. Most of the reported cases represented situations where the first appendectomy was done for appendicitis or abscess. The patients in this small group differ in that they had "prophylactic" appendectomies which, unfortunately, did not prevent future disease. In attempting to assess the problem objectively, we could only state that incomplete appendectomy was performed probably as a result of poor exposure of the appendiceal base and cecum. The fact that the exposures afforded in these three instances were primarily for regions other than the appendiceal area further supports this belief.

We conclude, therefore, that prophylactic appendectomy during operations for unrelated disease should not be performed unless the principles of good exposure and complete removal can be exercised. An individual with a subtotally amputated appendix may still develop appendicitis years later, and the added risk which he underwent in his primary procedure will have been in vain.

There is another lesson in these three case histories which is worthy of note. History of appendectomy does not rule out the possibility of a new episode of appendicitis. There is no substitute or simplifier to good clinical sense and judgment.

Summary

Three instances of appendicitis and its complications occurred in the retained stump of a previously amputated appendix. All patients had had appendectomy performed as a prophylactic procedure during operation for unrelated diseases. Such practices should be avoided unless the established surgical principles of good exposure and complete appendiceal removal can be carried out. A history of previous appendectomy does not rule out the occurrence of new appendicitis in a stump which may have been retained.

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THE FAMILY PHYSICIAN AND THE ADOLESCENT DELINQUENT

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In cases of adolescent delinquency the family physician may be called upon for help by the court, the parents, or even the child himself. The request for help can come from the adolescent even before he is in serious trouble, but it may be disguised in terms of concern for his bodily functions. In a society that is extremely critical of parents of delinquent children the parents have to deal with community feelings of disapproval as well as the troublesome behavior of their children. A vicious circle develops in which the parents treat their child as a bad person and the child becomes convinced that he has been rejected. Sometimes the physician can break this circle by emphasizing the positive personality attributes of all concerned. Some adolescents unable to develop close relationships with their parents are able to develop them with other adults, and such relationships, often informal, may be accompanied by rapid disappearance of delinquent behavior. Thus, there are many ways in which a physician can be of service to the delinquent and his parents, and many of these services are extremely gratifying.

The services of the family physician are frequently called on for help in understanding and treating the juvenile delinquent. Somewhere in the time between the onset of the child's first minor delinquency and his eventually becoming a serious problem to authorities, the physician may be expected to have some contact with the troubled child. This may come through the community, from the parents of the delinquent child, or, sometimes, from the child himself. Delinquency is only partly a medical problem and is usually dealt with more intensively by social workers, educators, or psychologists. The physician, however, is capable of exerting a strong positive influence in shaping the future development and behavior of the troubled child, even though his contact with the delinquent may be quite brief.

Why the Delinquent Is Referred to the Physician

The child who has been detected in antisocial behavior becomes a community problem and is referred to the juvenile court. The court has the responsibility for either sending the child to a training school or referring him for guidance to public welfare or probation workers. Public welfare and correctional agencies have decisions to make as to whether a child should be sent to a foster home or whether he or his parents should receive counseling or psychiatric treatment. In communities in which extensive psychiatric facilities are not available, the court will frequently call on the general practitioner for a statement as to the child's physical and emotional health. Public welfare or correctional agencies may also request examination by the family physician. Since community members have the responsibility for making important decisions, they are desperately in need of knowledge as to the child's emotional and physical state. Their knowledge of the presence of an illness, such as asthma, for example, would certainly influence decisions as to a foster home or a training school placement.

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It is to be expected that many parents will turn to their family physician when they are having difficulty with their child. The experiences of help and understanding they have received in the past reinforce their tendency to seek advice from the physician when they first learn they have a child with behavior difficulties. Many parents will bring their children to the physician with a request for a "check-up" or with rather vague complaints and then gradually and reluctantly reveal their difficulties. Few parents can readily admit that their child is in trouble and ask for help directly. More often they are wary and self-protective. Under the guise of concern for their child's physical health, they are looking for help in trying to understand his behavior.

Sometimes it is the child himself who seeks the physician's help because of results of deviant behavior. Thus, many adolescent girls who fear they are pregnant will first turn to their family physician as the only one they can trust. More rarely, boys who have been involved in fights or have become injured while participating in delinquent behavior will come to the physician first for assistance.

A request for help can come from the adolescent delinquent even before he is in serious trouble. Many adolescents are concerned with their deviant behavior, become guilty about it, and look for someone to talk to. They hope to find a neutral but responsible adult who is not as emotionally involved in the situation as their parents and who is willing to try to understand. It is natural that many of these children should turn to their family physician. A certain group of children will attempt to disguise their seeking help in terms of concern for their bodily functions. Thus, a child may come seeking advice for what at first sounds like a functional disorder. At other times there might be great concern for imagined inadequacies of physique and bodily development. Patient listening will sometimes reveal that the child is worried about his behavior difficulties.

Characteristics of the Adolescent Delinquent

Angry feelings toward parents, authority figures, and society in general are found in most delinquent children. Whether the physician is dealing with a sexually promiscuous girl or an uncontrollably aggressive boy, after a short period of listening it becomes apparent that they are in conflict with authority. While adolescence is usually a period of some rebellion even for healthy children, delinquents seem to display a disproportionate amount of resentment and distrust. They speak of the rules of society as being unfair, inconsistent, and discriminatory.[1] The same terms are applied to the way their parents treat them, often followed by some statement to the effect that "they don't understand me."

While all adolescents tend to be impulsive, the ability to delay the gratification of any impulse is quite weak in the delinquent. Since he is unable to delay acting on his impulse, the delinquent does not have the time to consider future consequences of his behavior or even to benefit from his own past experiences.[2] Usually the delinquent's offense is unplanned. Often he will state, "I took the money because it was there and I just wanted to" or "I don't know why I did it; I just suddenly decided I didn't care and I wanted to have sexual relations."

Another characteristic of the delinquent is his self-centeredness. He shows little interest in others or concern for their feelings. He seems to relate to people merely to manipulate or exploit them. Others are viewed with contempt or suspicion, except perhaps the few members of his delinquent gang. As a consequence, social relationships are superficial and of brief duration. Physical and psychological symptoms are common in the delinquent group of adolescents. Functional somatic complaints relating to all systems may be found. Preoccupation with alleged bodily inadequacies, particularly of the primary or secondary sexual areas, is prevalent. There is a lack of adequate defenses against anxiety. In a stressful situation, a delinquent may become aggressive or run away. If he can do neither, he is likely to experience a painful period of depression or anxiety. The delinquent may even distort reality, projecting his own inadequacies or forbidden impulses on to others, particularly adults and authority figures.

Etiology of Juvenile Delinquency

Juvenile delinquency is a complex problem involving cultural, economic, and psychological determinants. While the first two factors cannot be ignored in understanding this problem, this paper will be limited to discussion of the psychological factors.

The delinquent's impulsiveness, self-centeredness, and lack of defenses against anxiety form a syndrome indicative of extreme emotional immaturity. This concept is helpful in understanding the delinquent's behavior, much of which is more appropriate for a child of 6 than for a young adult of 16.

Another important concept, the role of unconscious motives in determining socially deviant behavior, has been clearly established by the psychoanalytic school.[3] Aichhorn[3a] has demonstrated that many children behave in an antisocial manner not because of any conscious desire for pleasure or economic gain but because of unconscious drives, such as the need for love or forbidden aggressive impulses.

Usually the patient's immaturity and unconscious conflict can be traced to mistreatment or rejection by one or both parents.[4] The child who is deprived of love and warmth cannot become a mature person and carries through his life a burden of hate.

Occasionally it is found that the patient's lack of inner controls is due to overindulgence by parents, who fail to set limits to the child's behavior. In still other cases, the parents seem to continually act in a way that encourages delinquent behavior on the part of their child while outwardly they may regret and condemn this behavior. In these cases it is felt that the parents are, in an unconscious manner, vicariously experiencing gratification of their own antisocial impulses through their children.[5]

A more subtle effect of the pathology of the child-parent relationship is the deep-seated feeling of guilt and worthlessness inculcated in the child. This feeling is usually unconscious, but it is easily discerned from the self-destructive nature of much of the delinquent's behavior. In fact, many authorities feel that a major cause of the delinquent's lawbreaking is, precisely, a sense of guilt and a corresponding need to be apprehended and punished.[6]

We feel that no matter how defiant the delinquent may appear, on some level he does have deep-seated needs for warmth and understanding. His previous relationships have been destructive, so that he is fearful of depending on anyone because he anticipates getting hurt again. Nevertheless, his dependency needs are so great that it is usually possible to break through the delinquent's façade of toughness and thus help him to achieve a feeling of being worthwhile. With this change in his self-concept, he can once again regain the ability to trust and cooperate with others.

Role of the Family Physician

When community agencies ask the physician to evaluate a delinquent adolescent, they are interested in receiving a thorough report of the child's physical condition plus whatever insights the physician can offer as to the emotional state. Physical defect that might lead to feelings of inferiority or of being "different" are important. A history of any type of neurological difficulty, particularly encephalitic attacks, should be noted. Any long-standing illness that has affected the patient's life situation significantly should be part of the information the physician passes on to the community worker.

While the psychological examination of the adolescent is difficult, many patients will talk much more freely with the family physician and will discuss symptoms that are clearly psychopathological. The adolescent changes rapidly in his mood and level of comfort and is liable to give information to one person that he would cover up in front of another. The physician may note the presence of anxiety symptoms, depression, hysterical somatization processes, or overt psychotic episodes. If agency workers are made aware of the presence of severe psychiatric symptoms, they may be helped to decide to have the child treated by a psychiatrist rather than following the usual case-work routine.

When the parents of the delinquent come to the physician, they are troubled with guilt, feelings of inadequacy, and a sense of helplessness. Often they tend to blame themselves secretly, but outwardly they project this blame on society. Such statements as "It's not Johnny's fault, it's just that everyone in town has it in for him" are common. The physician can be helpful if he accepts the parents' difficulties and allows them to discuss their troubles without being critical of them or their child. It is well to remember that our society tends to be extremely critical of parents of delinquent children. The parents have to deal with community feelings of disapproval as well as the troublesome behavior of their children. By the time parents of delinquent children come to the physician they are extremely sensitive. The physician must exert great caution to prevent the parents from seeing him as just another critical person who does not understand. Ventilation and clarification of problems can help relieve many of the parents' anxieties and keep them from acting in a manner that would worsen the situation.

It is important for the physician to help the parents accept what their child has done in a realistic manner. Some parents will tend to underestimate and belittle the trouble the child has had. In this type of situation the physician must help the parents accept the reality of what the child has done. Other parents will exaggerate the behavior of their children. The latter group calls their children incorrigible criminals, a description that is often far from realistic. Parents are sometimes relieved to find a reasonable adult who likes their child and who can emphasize his strong points as well as his weaker ones.

Parents who have dealt with a delinquent child for months and years have often forgotten about the positive qualities their offspring might have. A vicious circle then develops in which the parents treat their child as a bad person and the adolescent becomes more convinced that he actually is bad. This leads to further destructive behavior on the part of the adolescent and further rejection on the part of the parents. Sometimes the physician can interrupt this circle merely by reminding the parents of the positive personality attributes of their children.

Another area in which the physician can be helpful to parents involves acceptance of the decisions of community agencies. When the adolescent must be sent away to a training school, the parents are naturally disturbed. Their imaginations work overtime, and they picture the institution to which their child is sent as a punitive place which will make their son or daughter a hardened criminal. The physician can help explain the realities of the situation and point out that the child not only is receiving punishment but also is being given an opportunity to obtain professional help.

An agency recommendation for a referral to a psychiatrist must frequently be explained to parents. Some parents are more willing to accept their child as being "bad" than as being sick. They are liable to become extremely disturbed with the thought that their child needs a psychiatrist. In the segment of society from which most delinquents come a referral to a psychiatrist is often seen as evidence of insanity. There is much confusion and misconception on the part of lay persons regarding psychotherapy. Parents are naturally concerned with the lengthiness of psychotherapy and the need for confidentiality. Here again, the physician can be helpful by explaining psychiatric treatment and by stressing reasons for optimism.

The physician can be effective in several ways in his direct dealing with the adolescent delinquent. Reassurance as to physical difficulties or anatomic variations is often indicated. Adolescents have many misconceptions about their bodies and spend countless hours worrying about whether they are attractive or whether their sexual development is proceeding normally. Even the most sophisticated delinquent is often ignorant of basic information regarding physiology and hygiene, particularly with regard to sexual matters. It is amazing to find the number of teen-aged delinquents who actually believe acne is a direct result of masturbation. Simple explanations of bodily functions, particularly with regard to sexual development, can be reassuring.

A phenomenon frequently noted in the treatment of the adolescent is his ability to develop close relationships with an adult other than his parents, often in an informal way. These relationships, in a very impressive manner, are often accompanied by a rapid disappearance of delinquent behavior. In these cases the child discovers an "ideal," socially responsible figure who is also trustworthy and understanding. It seems almost as if the adolescent temporarily "borrows" the strength and moral code of the adult and is better able to control himself.[7] The physician is in a good position to become the adult friend or confidant of the adolescent. In these instances regularly scheduled "talks" between physician and patient can sometimes produce gratifying results.

As in the case of the parent, the adolescent may have difficulty in accepting the recommendations of the community with regard to treatment or referral to an institution. Again, the physician can help avoid the development of attitudes that might be permanently detrimental by patient and honest explanation.

It is our belief that pharmacological therapies have little place in the treatment of delinquency. Delinquent behavior does not seem to be attenuated by tranquilizers or sedative drugs and may actually be made worse. The child who receives tranquilizing drugs loses some of this ability to meet situations through active motor behavior and, in a sense, has had some of his usual defenses or outlets taken away from him. If this happens, feelings of restlessness, resentment, and inadequacy build up and may either lead to depression or erupt in antisocial behavior. Dependence on drugs is another complication in this group of patients, and termination of drug therapy is difficult. Tranquilizing drugs or barbiturates are indicated rarely and then only in situations where the child is experiencing incapacitating anxiety. They should be withdrawn as soon as the anxiety is under control.

Summary

While the treatment of delinquency is not entirely a medical problem, the physician is frequently called on to help the community, the parents, or the child in the evaluation of antisocial behavior. As long as physicians are looked on as persons with broad community interests they will be enlisted for this type of work. Delinquency is a complex problem related to social, cultural, and psychological factors. The adolescent delinquent is characterized by angry feelings, impulsiveness, self-centeredness, and many physical and psychological symptoms. Much of the delinquent's behavior can be understood in terms of his immaturity, his disturbed relationships with his parents, and his unconscious conflicts regarding feelings of aggression and sexuality. There are many ways in which a physician can be of service to the community as well as to the delinquent patient and his parents. Many of these services are extremely gratifying and lead to improved relationships between the community, the physician, and the family he treats.

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MEASUREMENT OF FREE ACID IN GASTRIC JUICE BY MEANS OF INDICATOR PAPER

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A pH test paper (Hydrion) was found to have the most favorable color scale over a pH range from 1 to 6, in comparison with many available indicator papers. Its use gives good correlation with the standard titration technique. Availability of a reliable, easily used indicator paper would encourage the physician to use gastric analysis more frequently and would stimulate patients to accept self-testing just as diabetics test for glycosuria.

Estimation of the amount of free hydrochloric acid in aspirated gastric juice by titration with a standard solution of sodium hydroxide dates back as far as 1886.[1] Simplification of this estimation has been attempted by the use of pH indicator papers. Using two indicators, Töpfer's reagent (0.5% solution of paradimethylaminoazobenzene) for a pH range of 1.4 to 2.0 and thymol blue for a pH range of 2.0 to 3.0, Denis and Silverman[2] prepared indicator papers for this purpose. Congo red paper has also been used in the estimation of free acid in gastric contents.[3] However, neither of these has proved successful enough to gain popular use. An investigation of the usefulness of a single indicator paper, having a broad color scale between pH 1 and 6, for estimating the amount of free acid in gastric juice is reported here.

Procedure and Results

Gastric contents were obtained by means of intubation 50 minutes after stimulation with use of Ewald's test meal. The amount of free hydrochloric acid was determined by titrating 10 ml. of gastric juice with 0.1 *N* solution of sodium hydroxide and with Töpfer's reagent used as an indicator. Results are expressed as degrees of acidity per 100 ml. of gastric juice, 1 degree being equivalent to 1 ml. of 0.1 *N* solution of sodium hydroxide. After comparison studies on samples of gastric juice, with use of many available indicator papers, a pH test paper (Hydrion) was found to have the most favorable color scale over a pH range from 1 to 6. To test the reliability of measurements with this indicator paper, the pH of six specimens having a range of free acid between 0 and 62 degrees was measured with a Beckman glass electrode pH meter. A good correlation was noted (table 1).

Sixty-two specimens were then analyzed for degree of free acidity and pH level. Table 2 lists the results in order of increasing amount of free acid. Examination of this table reveals a correlation between degrees of free acid and pH as measured with the indicator paper. Thus, when no free acid is present a pH above 4 is found. From 0 to 10 degrees of acidity corresponds with a pH between 3 and 4, from 10 to 30 degrees a pH between 2 and 3, and above 30 degrees a pH between 1 and 2. In table 3 are listed three examples of the use of the indicator paper in observing the change in gastric acidity of patients during a course of ulcer management.

Comment

The information obtainable by gastric aspiration can be of great usefulness to the clinician both in diagnosis and in the evaluation of treatment. Nevertheless, this time-honored procedure has in recent years suffered an unjustified decline in popularity. Our colleagues in radiology unceasingly remind us to correlate their gastrointestinal observations with clinical study, and yet there is a steadily increasing tendency for the clinician to base his conclusions almost entirely on the x-ray report.

This trend is in large part due to insufficient emphasis in medical teaching on the importance of studying gastric contents. Preoccupied with the more recent developments in diagnosis and treatment, we who serve on medical school faculties unconsciously tend to neglect the older and, to us, commonplace clinical methods. As one result, medical students frequently start their hospital experiences with little appreciation of the value of gastric aspiration. The Ewald tube, once as familiar to the intern as his stethoscope, has now become a strange and formidable apparatus, and his distrust and skepticism of the procedure often are reflected in the terrorization of the patient.

Witness the recent interest in "tubeless gastric analysis,"[4] which is sometimes proposed as an adequate substitute for true analytical methods.

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Certainly this is a worthy alternative in those rare patients in whom the passing of a stomach tube is contraindicated and, also, where the meager information that free hydrochloric acid is or is not present will suffice. This implication, however, that gastric aspiration is an unjustifiably difficult experience for the patient should be vigorously resisted.

Table 1.—*Comparison of pH of Gastric Juices Determined with Glass Electrode pH Meter and pH Test Paper*

	pH	
Degrees of Free HCl	Glass Electrode Meter	Test Paper
0	4.5	4-5
10	2.7	3
20	1.8	2
50	1.6	1-2
55	1.5	1
62	1.4	1

Rather than further discouraging gastric juice studies by promoting an inadequate substitute, we should consider means of simplifying the analytical technique, making it easy and practicable for the physician in his office. A reliable indicator paper, estimating the concentration of free hydrochloric acid, would eliminate most of the inconvenience, expense, and elaborateness now required to obtain this most useful of the chemical tests. So encouraged, the practicing physician would undoubtedly use gastric analysis much more frequently and derive benefit from the other information thus obtainable, as well as from the estimation of acidity.

Table 2.—*Correlation Between Degrees of Free Hydrochloric Acid of Gastric Juice and pH Measured with pH Test Paper*

Specimen No.	Free HCl, Degrees	pH	Specimen No.	Free HCl, Degrees	pH
1	0	5-4	32	20	2
2	0	6	33	22	2
3	0	6-5	34	23	2
4	0	4	35	25	2
5	0	5	36	28	2
6	0	6	37	32	2
7	0	6	38	32	2-1
8	0	6-5	39	36	2-1
9	0	5	40	40	1
10	0	6	41	42	1
11	0	6	42	42	1
12	0	5	43	43	1
13	0	5	44	43	1
14	0	5	45	44	2
15	0	6	46	45	1
16	0	5-4	47	47	1
17	0	5	48	52	1
18	0	6	49	52	1
19	4	3-2	50	53	1
20	5	4-3	51	54	1
21	6	4-3	52	56	1
22	6	3	53	56	1
23	8	4-3	54	58	1
24	9	3	55	59	1
25	10	3-2	56	60	1
26	12	3-2	57	60	1
27	13	3-2	58	62	1
28	14	3-2	59	64	1
29	14	3-2	60	70	1
30	18	3-2	61	75	1
31	20	2	62	85	1

A less frequent application of this simplified method for estimating free acid would be usage by patients with ulcers who test their own gastric juice. Those of us who follow the concept that complete neutralization of free hydrochloric acid is needed for optimum results in the medical management of peptic ulcer must, of course, train our patients to sample their gastric contents from time to time. Under this regimen, patients accept the necessity of testing for free acid just as the diabetic understands the need to check for glycosuria. Töpfer's reagent gives only the information that free hydrochloric acid is or is not present. Table 3 illustrates the manner in which the indicator paper would give these patients estimations showing their progress toward the ideal of complete neutralization and thus add greatly to their cooperative interest.

Table 3.—*Change in Free Hydrochloric Acid Level and pH During Course of Ulcer Management*

Case No.	Date	Free HCl, Degrees	pH
1	3/11	75	1
	3/16	58	1
	3/16	6	3
	3/19	0	5
2	3/15	85	1
	3/22	0	4
3	6/5	60	1
	6/7	56	1
	6/10	0	6

Summary

The determination of the concentration of free hydrochloric acid in gastric juice by the use of an indicator paper, having a broad color scale between pH 1 and 6, gives good correlation with the standard titration technique.

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Oksana Lyczkowskyj gave technical assistance in this study.

The pH test paper used in this study was supplied as Hydrion test paper by the Micro Essential Laboratory, Brooklyn, N. Y.

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BLOOD DISAPPEARANCE OF RADIOACTIVE ROSE BENGAL—RAPID SIMPLE TEST OF LIVER FUNCTION

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The rate of disappearance of radioactive rose bengal dye from the blood, determined by a simple counting method at the head, provides a sensitive test of liver function. Because dye levels do not depend on color comparisons, the test can be used despite the presence of jaundice. Multiple tests may be done without harm to the patient and can be carried out serially. One hundred five patients with various liver diseases were compared with normal subjects in this study. Results suggest that the test may supplement or replace the sulfobromophthalein test in the evaluation of borderline liver dysfunction.

The rate of disappearance of radioactive rose bengal from the blood, as determined by external scintillation counting, is a simple and sensitive test of liver function. It extends the usefulness of the present dye excretion tests to the entire spectrum of liver damage, thereby opening new possibilities in the study of liver and biliary tract disease. Such external counting over an area of blood [1] rather than over the complex liver area as done by others [2] greatly simplifies both the procedure and the interpretation of data.

The purpose of this paper is to describe techniques for obtaining the rate of blood disappearance by an external counting method, to establish the range of normal, to compare test results with those of other tests of liver function in certain disease conditions, and to explore areas for its use in clinical medicine.

Materials and Methods

Fasting patients were placed in a comfortable, supine position. A standard thyroid uptake scintillation probe, collimated by withdrawing the crystal 1-2 in. within a ½-in. lead shield, was placed against the right lateral part of the head, centered at the ear. After a background count was taken, 10-25 μc of radioactive iodine (I^{131})-labeled rose bengal in 2 to 5 ml. of isotonic sodium chloride solution and containing 0.1-1.0 mg. of "cold" rose bengal was injected intravenously so that the initial counts were about 10 times the background count. Counting rates were taken with a standard scaler every few minutes for 25 minutes. The net counts per minute were then plotted and the best line drawn through the obtained points.

Results

Comparison of Radioactivity at Head and in Blood.—Serial counts of radioactivity at the head and in blood samples were obtained simultaneously after the intravenous injection of 25 μc of radioactive rose bengal in a patient with jaundice and in one without (fig. 1). The blood and head count disappearance rates closely paralleled each other. Some separation occurred after about 20 minutes in the subject without jaundice, probably due to tissue binding and to activity reflected from the large abdominal concentration of dye. For testing purposes the head curve, obtained by external counting, and the curve of disappearance of the radioactive dye from the blood appeared to be equivalent.

Normal Values.—Quantitation of rate of dye disappearance from the blood may be made by comparing the radioactivity level at some early time to that at a later time. In order to select the most appropriate times for comparison of activity levels, typical curves were inspected. These revealed a rapid initial drop in activity (mixing phase), followed for about 20 minutes by a less rapid decline, after which the curve gradually flattened. Results in 95 normal persons were plotted with comparison of the radioactivity levels at 20:5 minutes, 15:5 minutes, and 10:5 minutes (fig. 2). The 20:5-minute grouping appeared to be most satisfactory for routine use since it provided time for blood mixing and adequate separation of normal from abnormal curves. The 20:5-minute comparison, expressed as a percentage, has been used in subsequent studies to indicate disappearance rate of dye from the blood. Normal values fell between 39 and 51%.

Reproducibility.—Serial tests were done during the fasting state in normal subjects and in patients with essentially stable pathological liver conditions. Reproducibility was consistently good (table 1).

Fasting Versus Nonfasting State.—To compare the fasting and the immediate postprandial states, tests were done on patients with normal and abnormal liver function. Food consisted of a heavy breakfast less than one hour before testing. Considerable variations occurred, usually in the direction of increased blood retention of dye in the nonfasting

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patient (table 2). Variations were more than would be expected from the reproducibility data. To standardize routine testing, subsequent patients were studied in the fasting state.

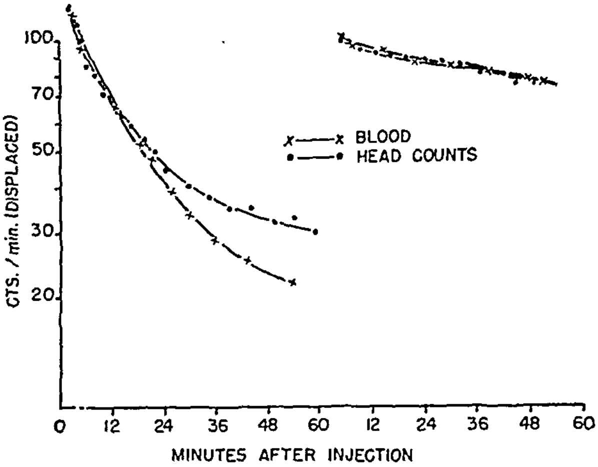

Fig. 1.—Radioactivity in serial blood samples compared with serial activity levels at lateral part of head after intravenous injection of 25 μc of radioactive rose bengal. Curves are displaced to start together at five minutes. *Left,* subject without jaundice; *right,* patient with jaundice.

Comparison with Sulfobromophthalein Test.—Comparison of results of the radioactive rose bengal and the standard sulfobromophthalein tests was made in several disease categories (table 3). In general, there is good correlation between the two procedures, both indicating approximately the same degree of dysfunction. There are instances, however, of the result of each test being abnormal when the other is within normal limits.

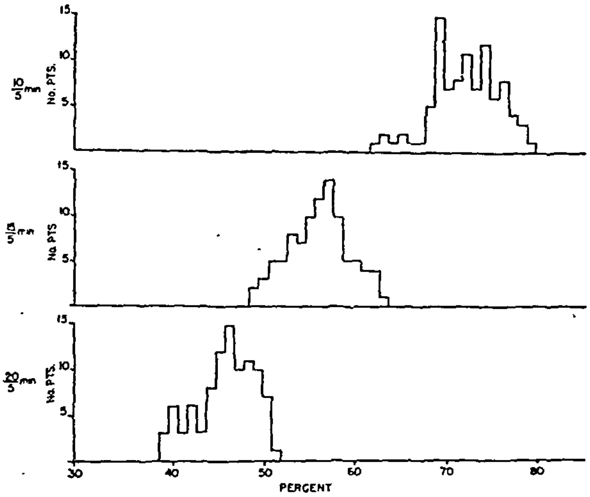

Fig. 2.—Results from radioactivity curves obtained at lateral part of head in 95 normal subjects, with comparison of dye activity retention at different time periods.

Serial Observations in Patients with Jaundice.—Data obtained by serially testing a patient with viral hepatitis are shown in figure 3. Rapid improvement in the rate of dye disappearance from the blood is demonstrated. Comparison of these results with standard liver function tests in the same patient is charted in figure 4.

Table 1.—*Reproducibility of Results in Serial Tests with Radioactive Rose Bengal in Normal Subjects and in Patients with Stable Clinical Conditions*

	Disappearance of Dye, 20:5 Min.					
	Test 1		Test 2		Test 3	
Case No.	Date	%	Date	%	Date	%
Normal						
1	9/27/56	49	4/24/57	49		
2	11/30/56	44	4/19/57	46		
3	11/29/56	44	1/ 3/57	45	4/15/57	45
4	11/14/56	41	11/28/56	40		
5	12/ 7/56	47	1/ 3/57	48		
6	12/18/56	48	1/21/57	46		
7	3/28/57	40	4/12/57	40		
8	10/18/56	39	10/25/57	45		
9	3/28/57	49	3/29/57	49		
10	11/29/56	44	1/ 3/57	45		
Alcoholism						
11	11/29/56	48	4/19/57	49	5/10/57	50
12	5/ 8/57	53	5/15/57	53		
13	11/29/56	47	4/27/57	47		
Cirrhosis of liver						
14	3/29/57	50	4/12/57	51		
15	11/ 2/56	51	11/28/56	52	1/ 3/57	52
16	10/ 9/56	65	10/19/56	64		
17	4/ 7/58	74	6/ 4/58	76	7/17/58	73
18	11/ 8/56	51	11/15/56	51	1/ 7/57	52
19	9/17/56	48	10/ 3/56	50	5/ 9/58	48

Clinical Conditions.—One hundred five patients with various liver diseases were compared with normal subjects. Figure 5 is a composite graph of the results. In cases where multiple tests were carried out in the same patient, only the first test result was recorded here.

Table 2.—*Fasting Versus Nonfasting State in Test with Radioactive Rose Bengal**

	Disappearance of Die, 20:5 Min., %	
Case No.	Fasting	Postprandial
Normal		
20	45	50
21	47	53
22	44	51
23	41	49
24	47	45
25	47	49
26	50	53
27	46	48
28	50	54
29	43	42
Cirrhosis of liver		
30	51	51
Alcoholism		
31	51	50
32	53	61
Chronic hepatitis		
33	49	49

* Food consisted of heavy breakfast within one hour of test.

Alcoholism.—The alcoholism group includes persons with known large alcoholic intake over a variable period of time but without physical stigmata of Laennec's cirrhosis. Results of the test with radioactive rose bengal fell above the upper limits of normal in about half of these patients.

Table 3.—*Comparison of Results of Radioactive Rose Bengal Test with Those of Sulfobromophthalein Test*

Case No.	Radioactive Rose Bengal 20:5 Min. %	Sulfobromophthalein*
Normal		
34	49	3.5
35	47	2.6
36	46	3.2
37	48	3.0
38	40	1.0
39	49	2.0
40	50	2.5
Alcoholism		
41	51	0
42	51	6.5
43	52	7.5
44	54	3.6
45	50	7.0
46	48	0.0
47	46	2.0
48	50	8.0
49	46	3.0
50	53	4.5
51	50	9.0
Chronic hepatitis		
52	50	7.0
53	52	2.5
54	53 51	12.0 5.0
55	57	8.5
56	42	6.0
57	57 50	4.5 4.5
Viral hepatitis, late		
58	56 48	11.3 2.5
59	56 49	11.9 5.0
60	59	14.0
61	45 43	6.7 6.0
62	57 49 47	10.0 9.0 7.0
63	55 55 48	15.0 13.0 12.0
64	57	14.0
Cirrhosis of liver		
65	51	10.0
66	50	3.0
67	52	3.0
68	52	4.5
69	50	14.0
70	51	10.0
71	45	3.0
72	58	28.0
73	65	30.0
74	79	33.0
75	51	8.0
76	67	28.0
77	59	28.0
Liver abscess, amebic		
78	56	3.5
Hyperthyroidism		
79	63	5.6
Hodgkin's disease		
80	50	4.0
Hepatolenticular degeneration		
81	50	6.0
82	57	9.0
Congestive heart failure		
83	54	23.0
84	62	16.0

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* 5 mg. per kg. of body weight at 45 minutes.

Laennec's Cirrhosis.—Patients with Laennec's cirrhosis had both a long alcoholic history and physical findings compatible with the diagnosis. Many had had liver biopsies. The disappearance rate (20:5 minutes) ranged from 48 to 96%.

Common Bile Duct Stones.—The group of patients with common bile duct stones includes only those in whom subsequent operation proved the presence of stones in the common bile duct, either tightly impacted or loose. Test results ranged from 53 to 87%; those in the upper range were in patients with jaundice.

Common Bile Duct Obstruction by Tumor.—Patients with clinically complete common duct obstruction for several weeks tended to have test results around 85%. Despite the presence of jaundice of up to seven weeks' duration, serial tests showed essentially no change (fig. 6). Of 16 patients with obstructing tumor, the only instance in which a value over 90% was observed was in a patient with cancer of the head of the pancreas completely obstructing the common duct. The result of the first test, 17 days after the onset of jaundice, was 84%, of the second, at 31 days, 84%, of the third, at 37 days, 86%, and of the fourth, at 51 days, when the patient had a fever of 102 F (38.8 C) due to a superimposed upper respiratory infection, 92%.

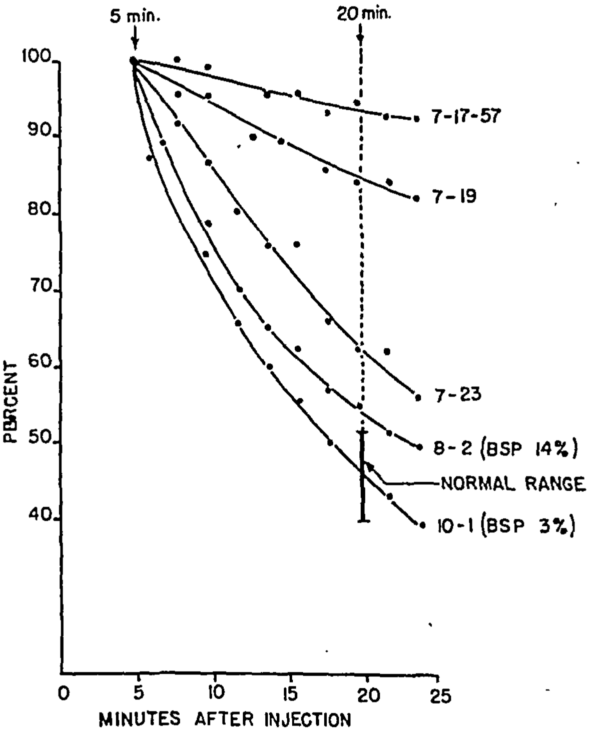
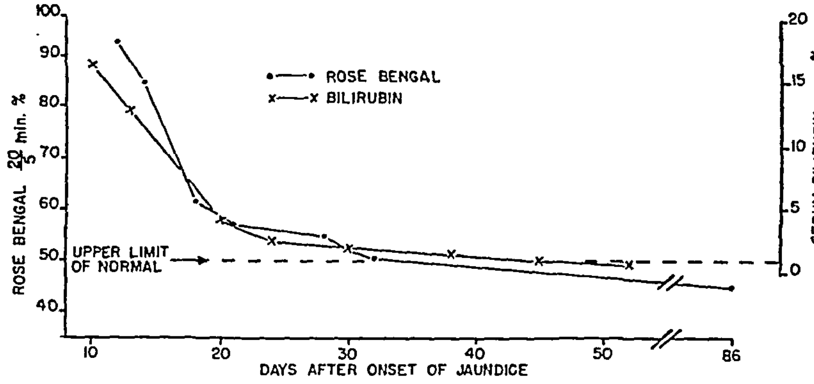


Fig. 3.—Serial test results on patient with viral hepatitis.

Comment

Dye excretion tests, with use of rose bengal and sulfobromophthalein, have demonstrated an excellent correlation with liver function in a large clinical experience.[3] These dyes are cleared from the blood by the polygonal cells of the liver and are then excreted through the biliary tract into the intestine. They provide the most sensitive indicators of borderline liver dysfunction. However, the value of both "cold" rose bengal and sulfobromophthalein has been restricted to liver disease without jaundice because of colorimetry problems and possible injury to an already damaged liver by large doses of dye.

The development of an I^{131}-labeled rose bengal has circumvented these problems. Since detection of changing concentrations of dye depends on levels of radioactivity rather than on color, valid results are extended to the entire spectrum of liver damage despite the depth of jaundice. Because of the minute quantities of both radioactivity and dye used, multiple tests may be done without harm to the patient even in the presence of complete biliary tract obstruction.



BSP			14	11		3
Alk p'tase	7.2		4.9	4.2	31	
CF (48h)	4+		4+	3+	2+	
T.T.	8		10	13	8	
S.G.O.T.		320	180	63	37	

Fig. 4.—Comparison of results of radioactive rose bengal test with those of other tests of liver function (same patient as in fig. 3). BSP = sulfobromophthalein, 5 mg. per kilogram of body weight at 45 minutes; Alk. p'tase = alkaline phosphatase level, Shinowara units; CF (48h) = cephalin flocculation at 48 hours; T. T. = thymol turbidity; S.G.O.T. = serum glutamic oxalacetic transaminase level (Umbright method, normal 5-40 units).

Most authors have followed the original method of Taplin and associates [2a] in attempting to obtain liver function data by external counting directly over the liver. The curves obtained have been interpreted as "uptake" and "excretion" rates, and attempts have been made to correlate results with the different causes of jaundice.[2] Except for estimating liver dysfunction, these efforts have been for the most part unsuccessful chiefly because of problems involved in external liver counting. When a scintillation probe is placed over the liver area it "sees" a complex of simultaneously occurring functions which may result in increases, decreases, or variable changes in radioactivity beneath the probe. These functions include dye uptake by the polygonal cells; blood flow to the liver; dye concentrations in blood of the liver and surrounding tissue; pooling of dye in the cholangioles, common bile duct, and gallbladder; and excretion of dye into the intestine. It is not possible to distinguish among these variables, and each may be changed appreciably by such factors as position,[4] exercise,[4] fever,[5] and food ingestion.[6] Further, the exact positioning of the scintillation probe may grossly change the shape of the curve,[2h] and body and organ movement make reproducibility difficult.

For these reasons we have chosen to obtain data away from the liver area (at the head and over the abdomen below the liver) and have found it to be quantitative and more free of complexity. External counting at the head detects the rate of disappearance of dye from the blood. This represents the "input" to the liver and is a function mainly of polygonal cell activity and liver blood flow. External counting over the abdomen below the liver detects the "output" of dye from the biliary tract into the intestine,[7] which is mainly a function of biliary tract patency. By the simple expedient of moving away from the liver we are therefore able to determine the ability of the liver to abstract dye from the blood on the one hand and the ability of the biliary tract to pass it along to the intestine on the other. We are concerned in this paper only with the first of these two elements.

To obtain the rate of disappearance of dye from the blood by the method of external counting over an area of blood, trials were made in several body regions. The lateral aspect of the head was chosen as the most appropriate site because it contains a rich and stable blood supply which is distant from the large and changing concentrations in the abdomen. There is a minimum of body and organ movement, providing a smooth and reproducible disappearance curve which correlates well with the rate of disappearance of dye as determined by blood samples.

Normal values are stated quantitatively by comparing the activity level at 20 minutes to 5 minutes as a percentage. From observation of many obtained curves, 5 minutes appeared to be the best time for a reference point, assuring good mixing of dye with the blood. Since the curve falls off in an essentially straight line for the next 20 minutes, the point of comparison could theoretically be taken at any point along the line up to 20 minutes. In patients without jaundice the curve falls rapidly; in these the 5:15-minute comparison would be adequate and would decrease testing time. However, as liver damage increases the curve becomes more horizontal and differences are made more evident by comparison to a later time. We have therefore chosen to use the 5:20-minute ratio expressed as a percentage as a standard test.

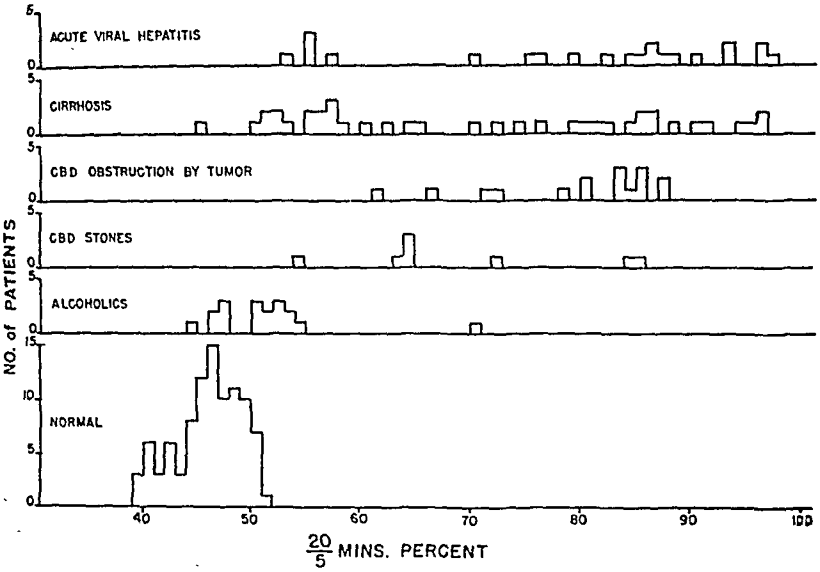


Fig. 5.—Comparison of results of radioactive rose bengal test in 95 normal subjects with those in 103 patients with various liver diseases.

The ingestion of food makes variable but distinct changes in liver and bilary tract function.[6] The rate of disappearance of the radioactive rose bengal tracer from the blood is usually decreased after food. Reproducibility of the blood disappearance test is much better under the standardized circumstance of fasting, and this has therefore become our routine procedure.

In borderline and moderate liver dysfunction without jaundice, the rose bengal tracer test and the standard sulfobromophthalein test appear to be about equal in demonstrating abnormalities. Results in patients with chronic hepatitis, alcoholism, and stabilized Laennec's cirrhosis are essentially the same, although each test appears to be more sensitive in certain persons. It is of interest that in serial studies of patients with viral hepatitis the rose bengal tracer finding becomes normal before that of sulfobromophthalein. At the present time there is insufficient evidence to determine whether one or the other correlates better with the true polygonal cell function.

In the differential diagnosis of jaundice this test has a definite, though limited, usefulness. The first important differential data are derived from serial testing (fig. 6). Since the main variable is polygonal cell function, it provides a method for direct comparison through the entire disease course. Rapid changes within a few days, usually in the direction of improvement, occur almost invariably in viral hepatitis. Such changes would in effect rule out extrahepatic tumorous obstructions of the common duct, Laennec's cirrhosis, and, in most instances, impacted common duct stones with jaundice. It is possible, however, that a stone which had passed or moved into a nonobstructing position would give the same results.

The second aid to the differential diagnosis of jaundice arises from the observation that patients with complete common bile duct obstruction by tumor have polygonal cell dysfunction on the order of 85%. Thereafter there does not appear to be any further deterioration of function, at least up to seven weeks of jaundice. On the other hand we have observed 12 patients with viral hepatitis or Laennec's cirrhosis with results over 90%. The only instance of extrahepatic biliary tract obstruction with a value over 90% was obtained in a patient who had a fever of 102 F at the time of testing, secondary to an upper respiratory infection (fig. 6). Since fever decreases polygonal cell function as determined by the sulfobromophthalein test,[5] it is reasonable to assume that the fever in this patient caused the additional failure of dye clearance. We presently consider that a value of over 90%, in the absence of appreciable fever, is high-

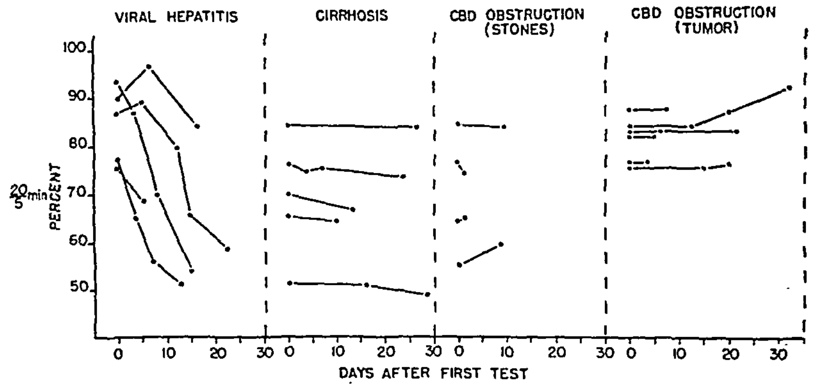


Fig. 6.—Results of serial tests with radioactive rose bengal in patients with various diseases.

ly suggestive of an intrahepatic lesion, most likely viral hepatitis or severely decompensated Laennec's cirrhosis.

Summary

presence of jaundice, thereby extending the useful-
The rate of disappearance of radioactive rose bengal dye from the blood, determined by a simple external counting method at the head, provides a sensitive test of liver function. In the evaluation of borderline liver dysfunction it may supplement or replace the sulfobromophthalein test. Because levels of the dye in the blood are detected by radioactivity rather than by color it can be used despite the ness of dye excretion testing through the entire spectrum of liver damage. Multiple tests may be done without harm to the patient even in the presence of complete biliary tract obstruction. The test can be used serially to follow the course of acute or chronic liver disease of any severity, and it is a useful adjunct in the differential diagnosis of jaundice.

Veterans Administration Center, Wilshire and Sawtelle boulevards (25) (Dr. Nordyke).

Lucille Shoop, R.N., Billie Jean Kinney, and Marianne Lederer supplied technical assistance in this study. Dr. Benedict Cassen, clinical professor of biophysics; University of California, aided in preparation of the graphs.

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ENURESIS.—The term enuresis should be restricted to children who wet the bed regularly, night after night, week after week, year after year. The wetting not infrequently seen in young children, 3 to 4 years of age, following birth of a sibling, is a transient phenomenon. . . . Enuretics ordinarily give a history of never having achieved normal urinary control. The history may be confusing, since parents not infrequently state that the child was dry until 5 or 6 years of age and only then began to wet. In most of these cases questioning will reveal that the children had been previously picked up during the night and placed on the toilet; when they are no longer picked up, they wet. . . . As a rule, enuresis, when untreated, persists into the adolescent years and then subsides spontaneously. . . . The emotional reaction of the enuretic to his symptom is influenced by the parent's attitude. . . . Discussions with the parents are designed to inform them about the nature of enuresis and about the futility and possible ill effects of undesirable attitudes. . . . The wetting is involuntary and no fault of the child's. Punitive attitudes . . . are useless and may be harmful. Such approaches . . . may intensify the wetting by unduly agitating the child, by rousing the negativism and, at times, by making him resistant and balky. . . . Explanations to the parents are best given in the presence of the child. . . . Conversations with the child should be directed toward building up his self-confidence and ridding him of feelings of hopelessness, shame and guilt. By relieving him of the burden of parental disapproval and, at the same time, giving him some understanding of the mechanism of his difficulty, nervous tension, which increases bladder irritability, is lessened. During treatment, discussion at home about the wetting should be limited to occasional encouragement and reassurance as improvement progresses.—H. Bakwin, M.D., Enuresis in Children, *The American Academy of General Practice,* April, 1959.

CLINICAL EVALUATION OF PELVICEPHALOGRAPHY

REVIEW OF 1,200 CASES

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and
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The advisability of routine roentgenographic measurements of the fetal head and maternal pelvis in obstetrics needs to be reconsidered because of the known hazards of ionizing radiation. In the years 1946-1947, among 702 patients, antenatal x-ray pelvimetry was used in 38.8%, while in the years 1956-1957, antenatal pelvimetry was restricted to 7.4% of the 597 patients. In the 1946-1947 series, 2% of the term babies were lost from conditions not related to the delivery, such as erythroblastosis and toxemia, while in the 1956-1957 series the term fetal loss was 0.8% from conditions not related to delivery. The decreased resort to x-ray pelvimetry did not increase the fetal risk. A series of 1,200 cases was analyzed in order to determine how helpful x-ray pelvimetry was in determining the need for cesarean section, and the evidence indicated that careful clinical study of the pelvis gave sufficient information in 70 to 80% of obstetric patients. Antenatal x-ray pelvimetry is therefore to be deprecated as a routine procedure, but it should not be witheld in critical situations.

It is agreed that the time-honored "external measurements" of the anterior superior iliac spines, iliac crests, and external conjugate give no reliable information regarding the pelvic inlet. At best, marked shortening of these measurements may hint that this inlet may be smaller than normal. The outlet may be measured accurately, and the subpubic angle may be evaluated. We are able, by painstaking vaginal examination in the last four to six weeks of pregnancy, to obtain fairly reliable information regarding the ischiatic spines, the pelvic walls, the sacrosciatic notches, the diagonal conjugate, and the sacrum. But we are not able to record accurate measurements of the information so obtained. Neither can we estimate accurately the weight of the fetus or the size of its head. But let us not discard this clinical study, for by its use a fairly accurate opinion may be formed regarding the feasibility of safe vaginal delivery in a given patient. In fact, as we hope to show, this will suffice for the majority of maternity cases.

It is logical that roentgenographic examination should be used in the search for accurate measurements of the various pelvic planes, and obstetricians and roentgenologists have collaborated in these studies. The technical difficulties have been overcome, and several systems of mensuration have been developed which give comparable results when properly used. Attempts have been made to establish critical levels dividing the field of feasible safe vaginal delivery from that in which such delivery is difficult or impossible. As will be shown, these attempts have not been as successful as we would wish.

Caldwell and co-workers,[1] in their monumental studies, have given a new and satisfactory classification of pelves based on careful x-ray measurements. Thoms[2] has done the same, using a different nomenclature. Each has subdivided pelves into four groups, with, of course, many pelves presenting many variations from the basic patterns. But the fundamental groupings are of great importance.

Recently, questions have been raised regarding the possibility of deleterious effects of radiation late in pregnancy on the mother and on the infant. Of course, the disastrous effect of heavy x-ray dosage on the fetus in the treatment of pelvic lesions in early pregnancy has long been known. But we have thought that the dosage of the diagnostic x-ray examination, especially when used late in pregnancy, was so small that no damaging effects were produced. However, the development of more accurate methods of measuring the intensity of radiation and recent studies on immediate and remote effects of radiation have cast doubts on these ideas. Stewart and co-workers,[3] at Oxford, studied English children under the age of 10 years who died of leukemia or other malignancies; the percentage of those subjected to antenatal abdominal radiation who died was 13.3, as compared to 7.4% in the living healthy children of the same age used as controls. Thus, of 547 deaths due to malignancy (269 leukemia, 278 other), prenatal abdominal diagnostic x-rays had been used 85 times, as compared to 45 times in the 547 healthy controls. Ford,[4] of Tulane University, has found the same to be true in Louisiana; her figures were 27.3% of children with leukemia and 29.5% of those with other malignancies (all under 10 years of age), as compared to 18.4% in healthy controls of the same age. She feels that the incidence in Louisiana of prenatal irradiation in utero is, therefore, about two and one-half times that in England. Interestingly enough, Stewart and associates found several

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groups of twins with one child affected and the other healthy. They feel that the diseased twin was no doubt anterior to the other when the exposure was made.

Table 1.—*Radiologic and Clinical Classification of 1,200 Pelves*

	Procedure		
	Radiologic		
Classification	No.	%	Clinical, No.
Gynecoid	861	71.75	243
Android	179	14.92	22
Anthropoid	120	10.00	15
Platypelloid	10	0.83	1
"Contracted"			54
Normal			695
Data not adequate	30	2.50	
Not studied			170

Furthermore, it has been suggested that this diagnostic radiation may have unfavorable genetic effects on the ovaries of the mother and the gonads of the unborn child. It is doubtful whether this question can be answered. We have delivered many women of healthy children after the first x-ray study and have delivered healthy children from several of these, with the second generation apparently as sound as the first. But mutations of the genes may not be manifest for many generations. At any rate, it would seem best to use x-ray pelvimetry only when definitely indicated.

In view of the uncertainties of clinical examinations, we began using x-ray pelvimetry some 25 years ago, at first in doubtful cases and later almost routinely in primigravidas and multiparas with poor obstetric histories. We were hopeful that the criteria to be considered would settle the matter of the type of delivery to be used, but increasing experience has shown that it is not possible to establish groups based solely on x-ray findings, dividing the expected deliveries into easy or difficult vaginal delivery and cesarean section. For several years we have resorted to the x-ray examination only when in doubt after careful clinical evaluation and have based our decisions in these doubtful cases on the x-ray and clinical findings considered together. Thus, in the years 1946-1947, of 702 patients, 272 had antenatal x-ray pelvimetry, whereas in 1956-1957 the total was 44 of 597. In the 1946-1947 group, 14 term babies were lost, in 4 of whom the loss might have been related to the delivery. In two of these four, the fetal deaths were due to prolapse of the cord in breech deliveries; the other two deaths were probably due to cord compression. The 10 other fetal deaths in this group were due to such conditions as hemolytic disease of the fetus and newborn (erythroblastosis), premature separation of the placenta (abruptio placentae), and hydrocephalus and, hence, were not due to bony pelvic abnormalities. In 1956-1957 the comparable figures were four and one. The latter death was probably due to sensitization by the D^u variant factor.[4A]

Results of Present Study

We are presenting a review of 1,200 cases, with the idea of assessing the real value of the x-ray studies and of comparing the radiologic and clinical findings. Dyer[5] presented a survey of 1,000 of these patients in 1949, showing the results when we were conforming rather strictly to the criteria accepted at that time. So the present approach is somewhat different.

Table 1 presents a listing of these patients according to the radiologic classification of Caldwell and co-workers.[1] Our percentages do not tally very closely with theirs; the difference is probably due in part to the fact that we arranged them on the basis of the x-ray measurements alone, whereas it would have been better to study the individual films as well. This was not done day by day, as the roentgenograms were taken, because of the press of work, and the majority of the films are no longer available. Furthermore, the patients under consideration were all Caucasian, seen in private practice, and of the upper social strata, in whom abnormalities due to dietary or environmental shortcomings were not to be expected.

In table 1 is also presented our clinical classification. As can be seen, we made little attempt to arrange the pelves from the scientific viewpoint but were chiefly concerned with the question of assessing them as to normality or deviations from the normal. We were chagrined to find that in 170 patients the pelvis was not carefully studied clinically. This occurred chiefly during the war years, when one of us (E. L. K.) was conducting a one-man private practice, in addition to his duties as head of the obstetric department of the college and of the associated hospital service.

In table 2 is a comparison of the radiologic and clinical findings as to normality of the pelves, regardless of the newer scientific classification. We found agreement in 724 cases, clinical error in regard to the midplane in 164 (110 on the conservative side), and insufficient data for comparison in 312.

It has been found, as noted by Dyer[5] and others, that inlet contraction alone is not so frequent as at the midplane and that outlet contraction exists only in combination with that of the midplane (and not often then). Table 3 shows the radiologic findings for the inlet and midplane. Of the 14 patients with both inlet diameters shortened, cesarean section was required in 6. In the midplane, we found 265 contractions of the transverse diameter (less than 10 cm.) and 161 instances in which the anteroposterior diameter was 11 cm. or less. However, of the latter only eight were of clinical significance, being less than 10 cm. (one was 8.5 cm. in a pelvis with

Table 2.—*Comparison of Number of Radiologic and Clinical Findings in 1,200 Pelves*

		Clinical		
	Radiologic	Normal	Small Midplane	No. Evaluation
Inlet and midplane normal	870	620	110	140
Inlet and midplane small	60	54	103	106
Inlet normal, midplane small	205			
Inlet small, midplane normal	25	25	2	2
Platypelloid	10	6		
Inadequate data	30			

all diameters small). All of these 8, and 31 of the others, were associated with shortening of the transverse diameter. In the remainder the slight degree of anteroposterior shortening was compensated for by an increase in the length of the transverse diameter. As is shown in table 3, shortening of the transverse diameter is associated with an increase in the section rate.

TABLE 3.—*Radiologic Findings in Patients with Shortened Diameters*

	Total No. of Cases	Type of Delivery	
		Vaginal, No.	Cesarean Section, No.
Inlet			
Anteroposterior 10.5 cm. or less	57		
Transverse 12 cm. or less	78		
Both	14		6
Midplane			
Anteroposterior 11 cm. or less	161*		
Anteroposterior and transverse	39		
Transverse 9.9-9.6 cm.	144	107	37
Transverse 9.5 cm. or less	121	62	59

* 8 less than 10 cm.

Criteria for Delivery

In attempting to establish radiologic criteria for the selection of the type of delivery in these pelves with decreased dimensions, attention has, of course, been paid to the fetal head. Mengert and Korkmas,[6] Savage,[7] and others feel that the head in the uterus cannot be measured accurately. Ball,[8] however, has devised a method of calculating the fetal head volume in vertex presentations based on the circumference at the level of the occipitofrontal plane, as determined by x-ray examination. This calculation really represents the volume of a perfect sphere of the given circumference. The fetal head, of course, is not a perfect sphere, but for practical purposes we can assume that it is and that it is attempting to pass the pelvic planes. Similarly, the volume capacity of the inlet and of the midplane is calculated from the shortest diameters of these planes. Torpin and Allgood[9] have found that fetal head measurements as determined by x-ray study are accurate. We have found, by measuring fetal heads (especially those of babies delivered by cesarean section and, hence, not molded) 24 to 36 hours after delivery, that the circumference checks very closely with that reported by x-ray examination; hence, we have concluded that the estimated volume reported is sufficiently correct for practical purposes. In breech presentation the location of the head precludes accurate measurement.

If the head volume is greater than the volume capacity of the pelvic planes, the difference is termed disproportion. The limit of permissible cephalopelvic disproportion at the inlet has not been dogmatically defined; however, at this level a trial of labor will settle the question. At the midplane, it is generally considered that a disproportion of 200 cc. is the upper limit of safety; however, we have learned by clinical trial that this is by no means invariably correct, especially when one is dealing with an otherwise normal pelvis. Dyer[5] believes that a head can mold safely to the extent that its cross-sectional volume is lessened 25%, permitting easier passage. However, if both inlet and midplane show deviations from the normal, a smaller degree of disproportion may be a barrier to safe vaginal delivery. We have delivered 11 patients vaginally since 1948 with midplane disproportion of 200 cc. or more—7 of these since 1952. The pelvis was anthropoid in nine and android in two. In one patient there was a discrepancy of 311 cc.; this patient was a secundipara who delivered spontaneously a child weighing 7 lb. 1½ oz. (3,217 Gm.). Sixty patients with midplane disproportion of 200 cc. or more were delivered by cesarean section—eleven after a trial of labor. We feel that 22 of the remaining 49 patients should have had a trial of labor. Interestingly enough, 9 of these 11 cases occurred after 1948, when we began to change our policy regarding these cases.

Mengert and Korkmas[6] have established indexes of the inlet and of the midplane which they feel are useful in predicting the possibility of dystocia. The anteroposterior diameter is multiplied by the transverse, and the product is divided by 145 for the inlet and 125 for the midplane (normals for those planes). If the percentage so obtained is over 85, there should be no difficulty. If it is below this figure, the possibility of dystocia increases as the percentage is lowered; at 70 or below in either plane 75% of the patients required section. The babies are classified simply as small, medium, and large. We feel that this index is of definite value, but we are of the opinion that some attention should be paid to the estimated head volume. Our experience with this index is shown in table 4.

Weinberg and Scadron[10] have devised another index. They add the anteroposterior and transverse diameters of the inlet and the transverse and posterior sagittal diameters of the midplane. The normals are 24.8 and 15.7 respectively. They state that if the former is 22 or less, or the latter 14 or less, delivery is usually accomplished by midforceps or by section. They found that if the inlet figure was 22 to 24 the head might engage, rarely if 20 to 22, never below 20, and also that delivery from below was rare with a midplane index of 13.5 or less and was the exception if it was less than 13. Our experience was somewhat different in regard to the midplane (table 4).

TABLE 4.—*Experience with Indexes of Mengert and Korkmas and Weinberg and Scadron*

	Mengert and Korkmas (Below 85%*)			Weinberg and Scadron						
					Inlet			Midplane		
Delivery	Inlet	Midplane	Both	No. of Cases	>22	21-22	No Data	>14	<14	No Data
Cesarean section, no.	6†	51	5	151	130	4	17	56	73	22
Vaginal, no.	3‡	32§	2						123‖	

* 1 vaginal delivery, indexes 80% and 79%, weight 5 lb. 12 oz. (2,608 Gm.); 1 vaginal delivery, indexes 100 6% and 61.4%, weight 6 lb. 12 oz. (3,062 Gm.).

† [illegible]

‡

§

‖ , 12; and 13.5-13.9, 70. All had inlet indexes of more than 22.

Value of Clinical Findings

We have discussed the question of the calculation of the head volume. We feel that it is necessary to stress the fact that there seems to be no correlation between this volume and the weight of the baby. A few illustrative cases are shown in table 5. It is interesting to note in passing that in cases in which the babies were rather large as compared to the head volume no trouble with shoulder dystocia was encountered.

As stated previously, we have used the pelvicephalogram much less frequently in the past 8 to 10 years, e. g., only 44 times in 1956-1957. As set forth in the tables, we have found that the various criteria proposed have been of some value, but our chief reliance has been placed more and more on careful clinical study. Roentgenograms have been made only in doubtful cases to aid in evaluation of the clinical findings. Kaltreider,[11] in many excellent papers, has stressed the value of clinical findings, trial of labor, and trial forceps in certain cases. Snow,[12] in his book published several years ago, strongly advocated x-ray pelvimetry but agreed that a trial of labor is frequently indicated.

Table 5.—*Head Volume and Weight of Baby*

Case No.	Head Volume, Cc.	Birth Weight, Gm.
85	600	2,976.7
107	640	2,523.1
379	614	4,280.7
6	635	4,422.5
305	549	4,309.1
141	695	4,535.9
411	784	4,904.4
404	803	3,798.8
365	840	3,401.9

In this series of 1,200 patients, we performed 151 cesarean sections; 150 were of the typical "low" flap type and 1 was extraperitoneal. In 44 patients with disproportion in whom trial labor failed, 14 had only moderate cephalopelvic disproportion. The failure of the head to engage may have been due to (1) a small inlet volume capacity (most of the x-ray reports did not give this figure), (2) faulty pelvic inclination,[13] or (3) unsatisfactory uterine contractions. There were 58 patients with disproportion in whom elective section was indicated, including 34 multigravidas; 5 had had cesarean section previously and 29 had histories of marked dystocia (many of the babies with birth injuries) and/or stillbirth. In 22 of the 39 patients with elective sections, we feel now that a trial labor was in order; these patients had disproportion of 200 cc. or more but might have been delivered vaginally. The 10 sections performed for other conditions (in patients with normal bony pelves) were for such conditions as fibroids, ovarian cyst blocking the pelvis, breech in elderly primipara, diabetes, and bleeding.

Thus, we see that section was performed in 12.58% of these patients studied roentgenographically. This, of course, is not the true incidence in our practice, as in the majority of our patients roentgenography was not done. Thus, in 1946-1947, 38.7% were so studied and the section rate was 10.1% (71 of 702), whereas in 1956-1957, 7.38% were so studied (44 patients) and the section rate was 7.2% (43 patients).

In this series of 1,200, there were eight stillbirths and two neonatal deaths in term deliveries. None was due to pelvic contraction, and no mother died. Causes of stillbirth included hydrocephalus, breech delivery; monster, multiple defects (2); macerated, cause unknown; macerated, cord tightly twisted; premature separation of the placenta; intrapartum death, probably cord compression; and prolapse of cord, double footling, in a primigravida. Causes of the two neonatal deaths were cerebral hemorrhage (midforceps) and probable sensitization to D^u variant.

Comment

From the review of our experience we feel that we can share the opinions of many others that clinical study of the pelvis will not always furnish information sufficient to serve as a guide in selecting the best method of delivery. However, we agree with Moloy [14] that if this pelvic examination is performed carefully and systematically we will need to use the x-ray in only 20 to 30% of our patients. This examination (preferably in the last three or four weeks of pregnancy) should cover the following points: measurement of the pelvic outlet; estimate of the subpubic angle, the mobility of the coccyx, the anterior surface of the sacrum, the pelvic walls, the sacrosciatic notches and ligaments, the ischiatic spine, the diagonal conjugate, the location of the presenting part, and an estimate as to the fetal size (large, medium, or small). If this examination leaves us in doubt, particularly if there is an associated history of marked dystocia in the case of a multigravida, a roentgenographic study is in order. We should bear in mind that the x-ray criteria do not resolve our uncertainties and that the decision rests on a study of all the findings, with, frequently, a trial of labor as the final recourse. It is evident from all that has been set forth in this paper that the x-ray study alone cannot be conclusive; hence, it is not wise for the roentgenologist to express an emphatic opinion regarding the probable obstetric outcome.

Summary

Studies now in progress seem to justify the suspicion that the incidence of leukemia or other malignant disease in early childhood may be slightly increased by the diagnostic use of pelvic x-ray examination late in pregnancy. It is theoretically possible that this mild radiation may produce mutations in the genes of mother or child, the effects of which may not be manifest for many generations.

Experience has shown that careful clinical study of the pelvis will suffice in 70 to 80% of obstetric patients. Roentgenographic pelvimetry is of great aid in a doubtful case but does not of itself determine the method of delivery to be used. Therefore, routine pelvicephalography is not recommended. However, it should not be withheld when it seems to be indicated, as the definite advantages more than offset the more or less theoretical disadvantages.

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PROBLEMS IN HYSTEROSALPINGOGRAPHY

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The diagnostic usefulness of hysterosalpingography was tested in a critical study of 395 cases. In each case the joint report of the radiologist and the gynecologist who carried out the examination was compared with subsequent findings of pathologists, specimens being obtained at operation in 486 cases. The reliability of the roentgenographic diagnosis depended much on the condition. The presence or absence of congenital anomalies was correctly reported in every instance, but the diagnosis of endocervicitis based on hysterosalpingography was substantiated in only 10% of the cases. Hysterosalpingography in this series was without value in endocervicitis and endometritis. It was somewhat more reliable in polyposis of the uterine cavity, ovarian cyst, endocervical polyp, fibromyoma, and ectopic pregnancy and most reliable in cases of congenital anomaly, carcinoma corporis uteri, and salpingitis.

Hysterosalpingography consists in roentgenographic studies after injection of radiopaque fluid into the uterus and fallopian tubes. The first attempt at roentgenographic visualization of the female genital tract was made around 1909. Since then many authors, mostly French and Scandinavian, have reported on this subject. There is no doubt that in recent years the value of hysterosalpingography as a procedure of diagnostic accuracy has been increasingly appreciated by radiologists as well as gynecologists. Yet we are still concerned with the frequency of radiologic misinterpretation, as borne out by operative and histopathological findings.

Nine hundred thirty-five hysterosalpingographic studies done in the radiology department of Notre Dame Hospital, Montreal, from 1952 to 1957, were carefully reviewed. This represents the total consecutive cases during that period of time. This diagnostic procedure has been in use at our hospital for the past 30 years. Clinical symptoms were correlated with roentgenographic and pathological findings in every case; clinical findings were taken

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from the patient's hospital chart, roentgenographic findings were checked and rechecked by two radiologists, and pathological findings were all checked and, in many problem cases, rechecked by two pathologists.

In order to avoid unnecessary repetition this paper will not deal with historical or technical facts or even with the well-known value of this procedure. The characteristic roentgenographic findings will not be enumerated or discussed. Names of many different authors associated with the evolution of hysterosalpingography can be found in the literature.

We believe that accurate interpretation of roentgenograms is only possible when the radiologist has sufficient knowledge of the patient's history to correlate the clinical findings with the findings on the film. But how well can he do it? What is the percentage of diagnostic accuracy in hysterosalpingography? The main purpose of this report is to attempt to answer this question.

Technique

Every examination was carried out jointly by a radiologist and a gynecologist. The technique was fairly uniform, with use of the uterine cannula, the fluoroscopic control, and iodized oil (Lipiodol) as the contrast medium. A follow-up anteroposterior roentgenogram was taken routinely after 24 hours. Of the 935 patients reviewed 486 or 52% were subsequently operated on. Among the operations performed were 65 laparotomies, 263 curettages, 111 hysterectomies, and 6 combined curettages and laparotomies.

Diagnostic Accuracy

Congenital Anomalies.—Congenital anomalies of the uterus are readily diagnosed by hysterosalpingography, as long as these anomalies can be placed in the broad classification suggested by Barnett.[1] His classification is based on appreciation of the contour and size of the uterine cavity. An accurate anatomic differentiation into the various subgroups described in textbooks of pathology cannot, of course, be made by hysterosalpingography, but if these subgroups are excluded, the rate of diagnostic accuracy in congenital anomalies approaches 100%. We found 21 patients with uterine malformations, representing a little more than 2% of the total examined.

Endocervicitis.—Two hundred twenty-one patients with endocervicitis diagnosed roentgenographically were classified into five morphologic groups, and every case was analyzed with regard to age, parity, time of examination relative to the patient's menstrual cycle, presence of leukorrhea, and other factors to determine whether any correlation could be drawn. Of these patients 46 subsequently underwent hysterectomy, and histopathological examination of the surgical specimens revealed a high rate of diagnostic error (90%), the radiologic diagnosis being substantiated in only 10%. Nor did there appear to be any correlation between the factors analyzed and the frequency of accurate diagnosis, there being a high percentage of false-positive diagnoses. It is clear that we overdiagnosed the condition, and it is our belief that accurate diagnosis of endocervicitis cannot be made radiologically.

Endocervical Polyps.—A total of 12 patients were examined for endocervical polyps, the diagnosis being suspected in 9. Of these, eight diagnoses were confirmed and one disproved, while in the remaining three patients the diagnosis was not suspected but was subsequently proved, in two by curettage and in one by hysterectomy, giving a rate of diagnostic accuracy of 65%.

Fibromyomas of the Uterus.—Fifty-four patients examined for uterine fibromyoma were submitted to hysterectomy; in 31 the diagnosis was correct, in 6 it was incorrect, and 17 patients with negative hysterosalpingographic diagnoses were discovered postoperatively to have fibromyomas, giving us in this series a diagnostic accuracy of 58%. The roentgenographic appearances of fibromyomas can be pathognomonic, but often small intramural fibroids and subserous fibromyomas will show a normal picture.

Cancer of the Corpus Uteri.—Cancer of the corpus uteri was suspected in six patients and confirmed in all at operation, a rate of diagnostic accuracy of 100%. This 100% does not mean that carcinoma of the corpus always presents a roentgenographically pathognomonic appearance. Four of these six patients showed characteristic signs of carcinomatous involvement, but the other two were merely sufficiently suggestive, on roentgenographic examination, that carcinoma had to be considered in the differential diagnosis.

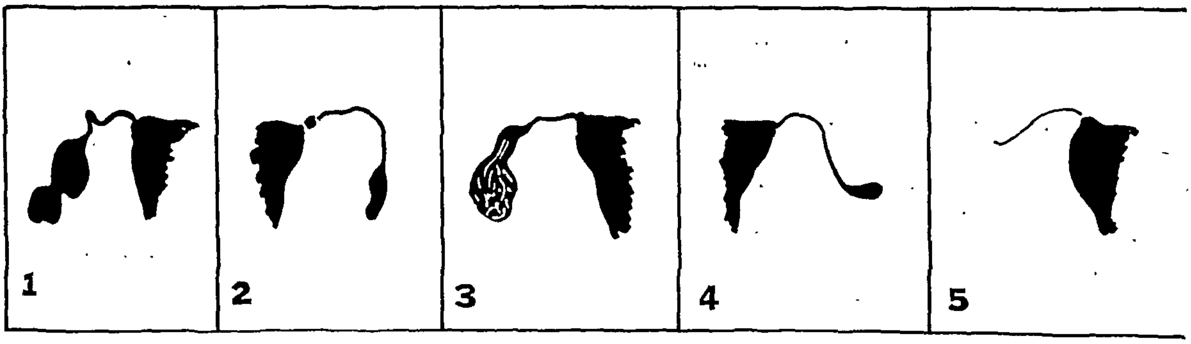
Polyps of the Uterine Cavity.—Of 22 patients suspected of having polyps of the uterine cavity by hysterosalpingography and subsequently examined pathologically, diagnoses were confirmed in 17. There were no false-negative findings, while in five patients fibromyomas rather than polyps were found, giving us a rate of diagnostic accuracy of 75%.

Ectopic Pregnancies.—In the series of 935 cases, four patients were suspected of having ectopic pregnancies, and all four diagnoses proved correct at operation. However, four other cases proved by operation could not be diagnosed by hysterosalpingography because of failure of opacification of the tube involved. If we consider these last four cases as diagnostic failures our rate of diagnostic accuracy of ectopic pregnancy was 50%.

Ovarian Cysts.—Twenty-seven patients had definite roentgenographic findings of an adnexal tumor mass suggesting ovarian cysts, but in four cases these findings were seen only on the 24-hour delay exposures. Surgery revealed 26 ovarian cysts and one tubo-ovarian abscess. However, of our postsurgical statistics 11 patients who had negative roentgenographic findings were found to have ovarian cysts, but 10 of these 11 tumors had a diameter less than 4 cm. Thus, on a total of 37 ovarian cysts and one tubo-ovarian abscess the diagnostic accuracy of hysterosalpingography was 70%.

Tubal Abnormalities.—Only 56 of 209 patients with tubal abnormalities, including salpingitis, hydrosalpinx, and tubal endometriosis, were subjected to surgery. Hysterosalpingograms showed 36 bilateral or unilateral lesions. There was complete failure of opacification in eight cases and unilateral failure of opacification in eight, the contralateral side being normal. Two false-negative diagnoses were also recorded. The 36 bilateral or unilateral tubal lesions suspected on roentgenographic examination were grouped in five different morphologic types (see figure). Salpingitis was diagnosed with accuracy in nine of nine patients of type 1 and seven of eight patients of type 2, for a combined rate of accuracy of 93%; but types 3 and 4, which according to certain reporters[2] should have demonstrated a high incidence of tuberculous salpingitis, showed no greater incidence of tuberculous over ordinary salpingitis (one of six patients of each type). Although the number of patients with proved pelvic tuberculosis is small in the present series, we believe that a firm diagnosis of this condition by hysterosalpingography cannot be made. However, the presence of so-called typical tubal changes can permit the radiologist to state the possibility of tuberculosis in the differential diagnosis.

Endometrial Hyperplasia and Endometritis.—The roentgenographic appearance in endometritis is not pathognomonic, and it is even less pathognomonic in endometrial hyperplasia. Here again, groupings were made according to the roentgenographic morphology in patients submitted to surgery. Thirty-six cases of endometrial hyperplasia and 61 of endometritis were classified according to these various types, based on irregularity of the uterine outline. There was little agreement between the roentgenographic observation and the pathological findings. Hysterosalpingography did not give any clue as to the differential histological character of these anomalies, and the rate of diagnostic accuracy cannot honestly be calculated. In the present series only one case of tuberculous endometritis was found after hysterectomy, and the hysterographic findings in this patient were entirely normal.



Morphologic types of tubal lesions.

Conclusions

It is evident that, when the problem is reviewed in this fashion, certain rates of diagnostic accuracy of hysterosalpingography are low. However, we believe that these percentages could be improved by a better selection of oily or water-soluble contrast mediums in accord with the clinical indications, and also by repetition of the examination in every case where complete bilateral failure of opacification occurred. We are aware of our low rate of detection of tuberculous salpingitis and tubal endometriosis, but after reviewing reports in the literature on these two subjects we wonder if these authors have not presented only cases in which the diagnosis was confirmed. The supposedly characteristic picture is, in our experience, far from characteristic, and the rate of accurate diagnostic predictability is extremely low.

Despite a background of 49 years of investigation and clinical use, hysterosalpingography is still struggling for proper recognition in many large medical centers. We believe that it should become a more widely used procedure. It is a safe and simple test and has a definite value in determining the choice of therapeutic measures to be followed. One should, however, be aware of its limitations as a diagnostic tool. In our series, although the rates of diagnostic accuracy were high for congenital anomalies (100%), cancer of the corpus uteri (100%), salpingitis types 1 and 2 (93%), and polyps of the uterine cavity (75%), they were less encouraging for ovarian cysts (70%), endocervical polyps (65%), fibromyomas (58%), and ectopic pregnancies (50%); for endocervicitis the procedure appears to be without value (less than 10%).

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IS ISOLATION OF INFANTS WITH THRUSH NECESSARY?

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Two types of physical facilities for handling newborn infants were compared with respect to the incidence of thrush (oral candidiasis) in 1,622 newborn infants. During the six months of the study three isolation periods alternated with three segregation periods. During segregation periods all infants with oral thrush were segregated on the side of the large general nursery. During isolation periods all infants with oral thrush were sent to the isolation nursery immediately on detection of the condition. Among 737 infants in the isolation group, 49 cases of latent or clinical candidiasis occurred; among 806 infants in the segregation group were 30 cases. The difference was not significant. The findings indicated that the advantages to be gained by physical isolation of infants with thrush are not commensurate with the direct and indirect cost of such procedure to the hospital.

In many municipalities oral thrush in the nursery for newborn infants is managed according to official regulations which require removal of infants with infectious diseases to a special isolation nursery. These regulations are partly based on the fact that many infectious diseases may spread by airborne transmission.

It is not generally realized that candidiasis differs from such diseases with regard to its pathogenesis and mode of transmission. It has been shown that maternal vaginal candidiasis is the main source of neonatal infection.[1] Newborn infants may harbor Candida albicans in the mouth and intestine for five to six days before the disease becomes manifest and the patients are removed to the isolation nursery.[2]

In many instances clinical manifestations of candidiasis appear only after the infants have been discharged from the hospital. In some cases the disease manifests itself only in its cutaneous form, which is frequently ignored both from the clinical and from the epidemiological point of view.[3]

In other words, unsuspected foci of candidiasis are always present in a nursery population, which escape the isolation regulations and constitute a potential source of general nursery infection.

Furthermore, it has been shown that candidiasis is not an airborne disease. C. albicans has not been isolated from nursery and hospital air or from soil and air in general.[4] Nevertheless, standard pediatric textbooks continue to refer to thrush as an airborne disease.[5] This concept leads to isolation of thrush cases in separate physical facilities. The space involved is costly, and the strain on the nursing personnel is considerable. In 1957, at Maimonides Hospital, Brooklyn, N. Y., the direct costs of nursing care alone for isolated thrush cases exceeded $2,000. The indirect expenses connected with isolation of these patients were estimated as considerable although no exact figures could be given. Inasmuch as the practice of isolation has been widespread throughout the United States for many years, it is obvious that considerable sums of money have been spent in this manner to prevent the spread of thrush in the general nursery. It was, therefore, deemed desirable to carry out an evaluation of the merits of isolating thrush patients in separate physical facilities.

Method of Study

Collection of Data.—The present study was carried out over a period of six months and comprised 1,622 consecutive newborn infants. During that time three isolation periods alternated with three segregation periods, each period comprising one calendar month. During the three segregation periods all infants with oral thrush were segregated on the side of the large general nursery. During the three isolation periods all infants with oral thrush were sent to the isolation nursery immediately on detection of the condition. The alternating periods were adopted due to the fact that the nursery facilities at Maimonides Hospital did not permit simultaneous study of two separate groups of infants. The presence of visible oral lesions, confirmed by direct smear, was taken as a criterion for isolation or segregation of the patient.

Oral smears and cultures for C. albicans were taken from every infant on the third day of life in order to detect potential cases of oral thrush.[2d] The tests were repeated on the seventh day. The average stay in the nursery at Maimonides Hospital is eight days for female and nine days for male infants. At that time clinical manifestations of thrush were

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usually present, while possible additional cases of "latent thrush"[2a] could be discovered before they were discharged from the hospital.

When the infants were 16 days of age, telephone inquiries were made of all mothers regarding the presence or absence of oral thrush. Affirmative or suspicious reports were verified as far as possible by a member of the research team who, with the pediatrician's and the mother's consent, visited the patient and took oral and stool cultures.

Table 1.—*Incidence of Clinical, Latent, and Delayed Thrush During Alternate Monthly Periods of Isolation and Segregation of Infants with Thrush*

	Isolation Periods					Segregation Periods				
	Duration, Mo.			Total		Duration, Mo.			Total	
	1	2	3	No.	%	1	2	3	No.	%
Thrush										
Clinical	8	7	7	22	2.9	8	4	5	17	2.2
Latent	4	4	11	19	2.4	5	3	1	9	1.1
Delayed	2	2	4	8	1.0	0	4	0	4	0.5
Total thrush	14	13	22	49	6.2	13	11	6	30	3.6
Total newborn infants	250	255	281	786	100.0	302	278	256	836	100.0

A record was kept of the daily census of the nursery and of the dates of admission and discharge of every infant. The daily census record was kept in the form of a map showing the location of every infant in the nursery. This daily map was devised in order to see whether the incidence of C. albicans would be higher among those infants whose cribs were immediately adjacent to that of a potential thrush patient and among infants who were cared for by the same nurse as the patient before segregation or isolation. The map, therefore, served as an indication of airborne or droplet infection and of possible transmission of C. albicans via the nurses' hands.

The possibility of airborne transmission of C. albicans was tested further by exposing Petri dishes with Sabouraud's agar for 24 hours in the immediate vicinity of thrush patients and at strategic points in the nursery. Petri dishes measuring 150 mm. instead of the conventional 100 mm. in diameter were used in order to increase the area of exposure. This experiment was repeated on three occasions, with a total of 60 plates, 12 of which were placed close to the patients' cribs.

Classification of Data.—Infected infants were classified into three categories: (1) clinical thrush—infants who developed clinical oral thrush while in the hospital; (2) latent thrush—infants who yielded C. albicans on culture while in the hospital, but did not develop clinical manifestations up to the 16th day of life; (3) delayed thrush—infants who developed clinical oral thrush between the day of discharge and the age of 16 days.

Table 1 summarizes the number of infants studied during the three isolation and the three segregation periods and the incidence of clinical, latent, and delayed thrush in the isolation and segregation groups.

Exposure Days and Average Exposure.—Each 24 hours or fraction thereof during which an infant with latent or clinical thrush was present in the nursery was counted as an "exposure day." This 24-hour unit of exposure was adopted since the exact time of onset of both latent and clinical thrush cannot at present be determined objectively.

If several infected infants were present in the nursery at the same time, exposure for those days was multiplied by the number of such cases. The average exposure to latent and clinical thrush was calculated separately for all infants in both the isolation and the segregation groups (table 2).

Comment

It will be noted from table 1 that the incidence of latent, clinical, and delayed thrush was higher in the isolation group than in the segregation group. However, the figures for clinical and latent thrush obtained for both groups fall within the normal range of incidence of oral infection at Maimonides Hospital, as determined in a previous study.[1b] These figures suggest that isolation procedures do not affect the normal incidence of thrush for newborn infants in the nursery and after discharge from the hospital.

The incidence of Candida infection was not increased in infants located next to, or in the same section as, infants with latent thrush. No cultures of C. albicans or other yeast-like fungi were isolated on any of the 60 plates that were exposed in the nursery while infants with clinical thrush were present. These findings indicate that the danger of airborne infection or transmission via the nurses is negligible.

Table 2 shows that exposure to clinical or to latent thrush did not affect the incidence of Candida infection. In both the isolation and the segregation group, the infants who developed candidiasis were exposed for approximately the same average length of time as those who showed no signs of infection. Although average exposure to clinical thrush was 50% shorter in the isolation group, the incidence of infection (6.7%) was almost twice as high as in the segregation group (3.7%). It will also be noted that exposure to latent thrush was considerable in

Table 2.—*Average Length of Exposure of Infected and Noninfected Infants to Clinical and Latent Thrush During Isolation and Segregation Periods*

	Isolation Group			Segregation Group		
	Infants, Total No.	Av. Exposure to Thrush, Days		Infants, Total No.	Av. Exposure to Thrush, Days	
		Latent	Clinical		Latent	Clinical
Infants without candidiasis	737	9.5	2.0	806	5.2	3.9
Infants with latent or clinical candidiasis	49	8.1	1.8	30	6.3	3.4
Incidence of infection, %	6.7	...	...	3.7	...	...

both groups. This is the type of infection which remains unsuspected and therefore escapes isolation procedures.

In table 3 a comparison is made of the incidence of Candida infection among infants who were and infants who were not exposed to clinical thrush during the entire six months of study. It will be noted that only 382 (23.5%) of the total of 1,622 infants studied were not exposed to clinical thrush while in the nursery and that the incidence of clinical and latent thrush was higher among the nonexposed infants. These figures illustrate again the lack of correlation between exposure to and incidence of Candida infection. Moreover, isolation procedures do not even protect the nursery population from exposure to the disease and thus fail in their main purpose.

The results obtained in the present study indicate that physical isolation of infants with thrush does not warrant its high direct and indirect costs to the hospital since such procedures neither prevent the occurrence of candidiasis nor protect the nursery population from exposure to the disease.

TABLE 3.—*Comparative Incidence of Candidiasis in Infants Exposed or Unexposed to Other Infants with Clinical Oral Thrush*

	Infants, Total	Infants Who Developed Thrush							
		Clinical (Before Discharge)		Latent (C. albicans Cultured, No. Lesions)		Delayed (Lesions After Discharge)		Not Infected	
	No.	No.	%	No.	%	No.	%	No.	%
Exposed to clinical thrush....	1,240	23	1.86	19	1.53	10	0 81	1,188	95.8
Not exposed to clinical thrush....	382	16	4.19	9	2.36	2	0.52	355	92.93

It has been shown repeatedly that the majority of newborn infants who develop candidiasis have contracted the infection at birth, before they were ever admitted to the nursery. Effective prevention of neonatal thrush, therefore, should begin with adequate therapy of the mother during the last trimester of pregnancy.

Summary

An isolation group of 786 and a segregation group of 836 newborn infants were compared as to incidence of candidiasis and average length of exposure to latent and clinical oral thrush. In the isolation group, all infants with oral thrush were removed to the isolation nursery. In the segregation group, all infants with oral thrush were segregated on the side of the general nursery. There was a higher incidence of candidiasis in the isolation group, despite a shorter average period of exposure to the disease, than in the segregation group. Less than one-fourth of the total number of infants studied in both groups were not exposed to clinical thrush in the nursery. The incidence of candidiasis was higher among nonexposed than among exposed infants.

There was no increase in the incidence of Candida albicans among infants located in the immediate vicinity of infected infants. No increase of infection was seen in infants handled by the same nursing personnel as infected infants. Attempts to isolate C. albicans from nursery air were unsuccessful. The danger of airborne infection or transmission of C. albicans via the nursing personnel therefore appears to be negligible. Isolation of infants with oral thrush in separate physical facilities does not diminish the incidence of the disease during the first two weeks of life. Moreover, these procedures fail to protect the nursery population from exposure to infection. Isolation procedures therefore do not warrant their high costs to hospitals.

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CLINICAL NOTES

ADENOCARCINOMA

UNUSUALLY LONG SURVIVAL TIME IN CASE OF KNOWN TUMOR RECURRENCE

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The behavior pattern of adenocarcinoma (hypernephroid carcinoma) is often bizarre.[1] It is not unusual for the tumor to become manifest by virtue of metastatic spread with the original lesion quiescent. We have seen two patients in whom biopsy of a bone tumor showed presence of adenocarcinoma, with the original lesion so small that it could not be revealed by intravenous or retrograde pyelography. Cases have been reported in which a solitary nodule appeared in the lung[2] and the disease was arrested for years by the removal of the original lesion and the metastasic growth. Within the past few years we have removed a carcinoma of the kidney with multiple metastases in the lungs and one tibia. Aided by roentgenologic therapy to the bone, there has been partial regression of the metastases, enabling the patient to walk with the aid of a cane and to resume a gainful occupation. The disease seems to have become quiescent. The case reported on here we believe worthy of attention because of an extremely long period of survival in the presence of known tumor recurrence.

Report of a Case

This patient was first admitted to Michael Reese Hospital, Chicago, on April 14, 1943, with the complaints of hematuria, nocturia, and polyuria. These symptoms had been present for a number of months. Six years previously he had symptoms of renal colic, and in 1918 an attack of influenza had left him with severely impaired hearing. His father died of carcinoma of the prostatic gland and an aunt died of carcinoma of the stomach.

Physical examination revealed a well-developed, well-nourished, 51-year-old man who was quite deaf. The significant physical findings were a slight enlargement of the liver and the presence of an ill-defined mass, that moved with respiration, in the left upper quadrant. There were external hemorrhoids, and the prostate was not enlarged. Cystoscopy was carried out with the patient under local anesthesia. The bladder was not remarkable, and both ureters were readily catheterized. The function of the left kidney was somewhat impaired as compared to that of the right, with the use of indigo carmine as an indicator. Bilateral pyelography was carried out and showed the presence of a space-occupying lesion of the lower pole of the left kidney. The left kidney was exposed surgically and the lower pole found to be the seat of a large tumor. A nephrectomy was carried out and the patient made a good recovery from the operation. Gross and microscopic examination confirmed the diagnosis of adenocarcinoma. No radiation was given postoperatively.

The patient remained well until March, 1949. At this time he had an attack of pneumonia. On his recovery he went to his phyician's office and, during fluoroscopy, suffered an attack of syncope, falling to the floor. At that time the abdomen was extremely flaccid and, when palpated, revealed the presence of a large mass deep in the iliac fossa. It was almost impossible to palpate this mass when the abdominal muscles were normally tense. On x-ray examination the colon was found to be displaced medially by a retroperitoneal mass. A transperitoneal exploratory operation was carried out and the mass exposed by incision of the posterior peritoneum lateral to the descending colon. A fairly well-encapsulated mass was found adherent to the posterior abdominal muscles, through the middle of which the stump of the ureter coursed. The entire mass was removed with adherent muscle and fat and with the ureter down to the bladder. The microscopic picture of the specimen was that of adenocarcinoma and agreed in detail with that of the original tumor removed six years before. The patient made a good recovery from the surgical procedure.

The patient was seen only infrequently in subsequent years until he returned in July, 1955. At that time he was suffering from progressive loss of weight and running a low-grade fever. Physical examination revealed the presence of an extremely large and fixed mass that seemed adherent to the posterior abdominal wall. On x-ray examination the colon was displaced to the midline. At surgical exploration a tremendous mass was found occupying the left retroperitoneal region extending from the diaphragm, to which it was densely adherent, to deep into the true pelvis. There seemed to be no possibility of successful removal,

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so a piece was removed for biopsy and the wound closed. In spite of the known resistance of this type of tumor to radiation,[1a] several courses were given and we were gratified at the response. There was a perceptible decrease in the size of the tumor, and the temperature returned to normal. Several blood transfusions were given. The patient regained his normal weight and when last seen in February, 1959, had no subjective complaints. On examination there was still a large mass in the left side of the abdomen, but it was apparently causing him no trouble.

This type of adenocarcinoma is altogether unique in our experience. It is apparently only locally malignant and has no tendency to metastasize to distant points. Fifteen years have elapsed since the original nephrectomy, and there seems to be no question but that tumor has been present during this entire period.

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NEW, RAPID METHOD OF OBTAINING DRY, FIXED CYTOLOGICAL SMEARS

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Since Papanicolaou[1] first described a procedure of preparing smears for cytological examination numerous investigators have attempted to improve the method of fixation. Their principal purpose was to achieve good preservation of cells with a minimum time spent in fixing the slides and a convenient and safe means of transporting these slides to the laboratory.

The original method consisted of placing freshly prepared smears into a bottle containing a mixture of equal parts of alcohol and ether. The cellular fixation resulting from this method is excellent, and it is still being widely used even though the bottles are bulky, subject to breakage, and not suitable for mailing. Several workers have made innovations principally in order to render the slides amenable to transportation in a dry state.

Ayre and Dakin[2] suggested fixing slides in alcohol-ether and then covering them with glycerine and another clean slide. Sagi and Mackenzie[3] described a method of fixing smears by immersing them for 10 to 30 minutes in a 90% solution of acetone and permitting them to dry. Papanicolaou[4] used a synthetic resin (Diaphane) dissolved in alcohol which dries in 20 to 30 minutes when applied to a wet smear. In the laboratory the resin must be removed from the dry slides before staining by placing them into an alcohol-ether mixture for 20 minutes.

Nieburgs[5] advises mailing nonfixed dry smears, which are then rehydrated in the laboratory before staining. The nonfixed smears are said to be satisfactory after a period of as long as two weeks. When received in the laboratory these dry smears must be placed in a rehydrating fluid for one to five minutes and rinsed in equal parts of 95% concentrations of alcohol and ether. Then they are fixed for 10 minutes in another 95% alcohol and ether mixture and run down through alcohol concentrations (95%, 70%, and 35%) and distilled water before they are ready for staining.

Sills[6] first described a method of fixing slides in alcohol-ether and then dipping them into melted polyethylene glycol 1540 (Carbowax compound 1540). The latter forms a tough protective coat on the smears. Later, Sills and Garret[7] developed a method whereby the polyethylene glycol was added directly to the alcohol-ether mixture. Freshly prepared slides were placed in a bottle containing this solution for 30 to 60 minutes and then removed and dried. During this process the smears were fixed and covered with polyethylene glycol in one step.

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After using the techniques described above, we concluded that the ideal procedure should comprise the following points: (1) good cellular fixation and preservation, (2) ease and rapidity of fixation, (3) elimination of cellular contamination or artefacts by the use of common fixing container and fixing fluid used for several cases, (4) as the end-result, dry smears which can be readily mailed, (5) the avoidance of further complicating the staining procedure by additional steps of rehydration or removal of material, and (6) economy. The method to be described here has proved to be completely satisfactory and fulfills the criteria enumerated above.

Method

Freshly made smears are placed on a flat surface and flooded with a fixing solution. The slides dry in five to seven minutes, and an opaque waxy film forms on the surface. Slides with a 0.75-in. fine grain frosted surface at one end are preferable. The patient's name, as well as the origin of the material (i. e., vaginal, cervical), is noted in pencil on this surface. This eliminates the use of metal clips and other cumbersome methods of identification. The slides may then be placed in a suitable mailing container for transportation to the laboratory.

The fixing solution is made up of equal parts of 95% concentrations of alcohol and ether to which a 5% solution of polyethylene glycol is added. In order to facilitate the preparation, polyethylene glycol is placed in a 56-C incubator until it becomes soft. It is then added to the alcohol-ether mixture. A uniform, clear, and stable solution is obtained after standing for several hours. The dissolution of the polyethylene glycol may be hastened by agitation. The fixing solution, which is prepared in the laboratory, is then divided into small glass dropper bottles for distribution.

The dried slides prepared in this manner may be placed directly into hematoxylin without previous treatment. It is not necessary to remove the polyethylene glycol, which is soluble in water as well as in the alcohol-ether mixture.

Experience with This Method

We have found this method to be simple and rapid. By the time the patient is ready to leave the examining room, the smears, which were flooded with the fixative, are dry and ready for processing or transportation. The slides may be stored for several months without deterioration. They can probably be kept indefinitely.

Slides prepared in this manner and stained with the Papanicolaou staining procedure[1] give excellent results. The stained slides are entirely comparable and in many instances superior to slides fixed and kept in alcohol-ether containers. The female-sex chromatin is clearly visible and sharply delineated in numerous nuclei. This is considered to be indicative of the excellent technical quality of the fixation.

Each slide is flooded separately so that there is no possibility of cells being washed off from one slide and then being caught on subsequent slides from another patient. This problem may arise when a common container is user repeatedly to fix or coat slides. Slides prepared in this manner do not require rehydration or additional treatment to remove the waxy coat in the laboratory, since polyethylene glycol is water soluble and will dissolve when placed directly into hematoxylin. The accumulation of dissolved polyethylene glycol in the staining solution does not interfere with the staining.

The method is economical, since only a few drops of the fixing fluid are needed for each slide.

This technique may be used for cytological smears made of any material or fluid, such as vaginal, bronchial, sputum, pleural, or peritoneal. It is also suitable for sediments of centrifuged fluid.

Conclusions

A method for rapid and simple fixation of cytological smears requires only a few drops of fixing solution for each slide. There is no possibility of cellular contamination, the fixed slides are dry and may be mailed, and the method is economical.

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The polyethylene glycol used in this study was supplied as Carbowax compound 1540 by Union Carbide Chemicals Company, Division of Union Carbide Corporation, New York.

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ERYTHEMA NODOSUM AS A MANIFESTATION OF HISTOPLASMOSIS

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Erythema nodosum is a reaction pattern of the skin characterized by the formation of symmetrical, nodular, erythematous, painful, and tender swellings on the pretibial surface of the legs. Less frequently, the lesions may appear on other parts of the body. The cause is not always determined but is usually a manifestation of an infection or drug eruption.[1] Although erythema nodosum is not an uncommon manifestation of a deep fungal infection, such as coccidioidomycosis,[2] to our knowledge there has been no reported association of this syndrome with histoplasmosis. The purpose of this report is to describe erythema nodosum occurring as a manifestation of histoplasmosis.

Report of a Case

An 18-year-old girl from Copenhagen, Denmark, was admitted to University Hospital on Jan. 7, 1958, with a "rash" on her legs of five days' duration. Ten days before admission she began to experience moderate intermittent headaches which required no therapy. Five days before admission she noted the appearance of large, raised, tender areas over the extensor surfaces of the lower part of both legs. At this time she also had mild anorexia. The day before admission she experienced generalized malaise and discomfort in the angles of her jaws as well as bilateral conjunctivitis.

Her history revealed that she had had mumps in 1945 and infectious mononucleosis in 1956. Otherwise, she had been in excellent health. There was no history of allergy. The patient had come to the United States three months previously, when she enrolled at Ohio State University in late September of 1958. At that time, as part of a program at this university, she was given skin tests with both purified protein derivative (PPD) and histoplasmin. Her tuberculin test gave a positive result and the histoplasmin test a negative result. Chest x-ray was normal.

Physical examination revealed a well-developed, well-nourished girl in no acute distress. Her temperature was 99.6 F (37.4 C) rectally, pulse rate 90 per minute, respiration rate 20 per minute, and blood pressure 120/80 mm. Hg. Positive physical findings included bilateral conjunctivitis and, over the pretibial areas of both legs, raised, nodular, erythematous, tender lesions measuring 2 to 4 cm. in diameter. The rest of her physical examination was not remarkable.

Hemogram on admission revealed a white blood cell count of 11,400 per cubic millimeter with 71% neutrophils, 23% lymphocytes, 4% eosinophils, and 2% monocytes; hematocrit value 43%; and hemoglobin level 13.6 Gm. per 100 ml. Urinalysis gave normal findings. Throat culture showed no pathogens. Antistreptolysin and heterophil agglutinations gave negative results, as did serologic tests for syphilis. The yeast-phase complement-fixation test for histoplasmosis[3] showed negative findings, but the histoplasmin collodion agglutination test[4] gave a positive result with a 1:40 titer. The histoplasmin skin test gave a positive result with induration and edema measuring 30 mm. in diameter after 48 hours. The second PPD test also gave a positive result after 48 hours. A chest x-ray taken on admission showed mild bilateral adenitis and some evidence of pneumonitis in the medial segment of the middle lobe of the right lung. A repeat collodion agglutination test done one week later again gave a positive result with a 1:40 titer; the complement-fixation findings remained negative. A single bone-marrow culture and three blood cultures showed negative results.

The patient was treated symptomatically and was afebrile throughout her hospital course. She was discharged on the 13th hospital day, at which time the lesions on her legs were still present, less painful, and somewhat darker and smaller.

Comment

Histoplasmosis and histoplasmin sensitivity are rare in Denmark.[5] In fact, only 0.6% of an average population in the eastern part of Sweden are histoplasmin-positive. The patient who came from Copenhagen had shown negative results on skin tests with histoplasmin on admission to Ohio State University three months prior to her present illness. The conversion of her skin test findings from negative to positive occurred within a three-month period of residence in Columbus, Ohio, an endemic area.[6] In addition, two separate serum specimens from this patient showed positive collodion agglutination reactions at 1:40 dilutions. Another factor compatible with the diagnosis of histoplasmosis was the hilar adenopathy and pneumonitis in the middle lobe of the right lung. In view of the fact that the patient was afebrile and relatively asymptomatic except for her local skin lesions, failure to recover Histoplasma capsulatum from a single bone-marrow culture and three blood cultures is not inconsistent with the diagnosis. The dissociation of serologic results with positive collodion agglutina-

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tion findings and a negative complement-fixation result has also been observed in this laboratory on other occasions.

The manifestations of histoplasmosis are protean.[7] Erythema nodosum is a well-accepted component of the systemic fungus infection of coccidioidomycosis, which is endemic in the southwestern part of the United States. It seems reasonable to assume that it could occur in patients with histoplasmosis, which is endemic in the eastern central states. A high index of suspicion and inclusion of studies for the diagnosis of histoplasmosis will probably result in the recognition of histoplasmosis as an additional etiological agent associated with the syndrome of erythema nodosum.

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COUNCIL ON DRUGS

Report to the Council

The Council has authorized publication of the following paper, which was presented as part of a symposium-panel discussion held in Washington, D. C., Sept. 25, 1958, on the Use and Abuse of Adrenal Steroids. This is the third paper in the series, the first and second of which appeared in The Journal *on June 20, and 27, 1959, pp. 951 and 1063.*

H. D. Kautz, M.D., *Secretary*

STEROID THERAPY IN SYSTEMIC INFECTIONS

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We are all familiar with the tendency of the adrenal cortical steroids to alter manifestations of a variety of clinical disorders, and, of course, these include infectious diseases. This was studied and strikingly demonstrated by Finland and co-workers[1] when the adrenal cortical steroids were given to carefully selected patients with lobar and viral pneumonias. These observations made it clear that the steroids could induce, in patients with pneumonia, striking defervescence and symptomatic relief, with a decrease or disappearance of not only the subjective signs but also the objective findings. These remarkable changes occurred despite the persistence of pneumococci in the sputum, the presence of bacteremia, and, in one instance, the spread of pneumonia to other lobes with subsequent development of empyema. The symptomatic changes apparently were independent of gross changes in the antibody response and were not accompanied by reversal of metabolic patterns consistent and characteristic of pneumonia and other severe trauma. Subsequent to the initial reports, many clinical and laboratory data have accumulated,[2] which attempt to answer some of these observations. There are several broad questions which as yet have not been answered. Are steroids really valuable in infectious diseases or useful in any particular area of infectious diseases? Since these agents may not be helpful, but may be harmful, can one be specific in their use, so that the advantages may be obtained without serious consequences?

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Early in the study of these problems,[3] these agents, without antibiotics, were used in a variety of infections such as tuberculosis, typhoid, bacterial pneumonia, and bacterial endocarditis. Certain objective information was obtained from these studies. Steroid therapy used in these patients with acute febrile illnesses brought about rapid remission and reversal of the distressing clinical evidences of the illness. When the etiological agent could be demonstrated, as in bacterial pneumonia, typhoid, and subacute bacterial endocarditis, despite the remission of the clinical syndrome, there was frequently noted evidence of increased multiplication or spread of the micro-organisms.

The ability to detect the depression of immunity is difficult, and many of the disease syndromes for which patients are treated with steroids are the type in which the mortality is low and complications are infrequent. However, in certain areas, controlled studies have been helpful. For example, in infectious hepatitis, the use of steroids leads to rapid symptomatic improvement and a rapid fall in level of serum bilirubin. However, it has been shown that relapse occurred in 20% of the treated patients and did not appear in controls.[4] The hormone should not be employed in the average case but only for patients who are quite ill, especially those with marked anorexia.[5]

The effects of steroids were observed in a controlled study on the course of poliomyelitis,[6] as well as in acute streptococcic disease,[7] and indicated no particular effect on the acute disease or on the sequelae. There were no adverse or favorable effects.

The effect of steroids in mumps orchitis is controversial. There have been reports of rapid remission subsequent to their administration; on the other hand, controlled studies have indicated no difference in response to corticotropin (ACTH, Acthar, Corticotropin, Cortrophin) or a placebo.[8] However, in these controlled studies the doses were not very large.

The occurrence of infections as aggravations of preexisting ones or spontaneously in patients receiving steroids during treatment for other conditions is well known.[9] This occurrence has been a major factor in complete or partial cessation of therapy with these agents. We should be aware of the need for judicious observation before administering the steroids, particularly in patients in whom pulmonary tuberculosis might be present.

The degree of hazard of infection in patients receiving corticosteroids is not easy to evaluate. These agents may so camouflage the appearance of septicemia that the infection may only be noted at autopsy. There have been instances in which steroids were used in patients with fever of unknown origin, with the assumption that an infection rather than tuberculosis was present, only to have rapid progression of active tuberculosis, indicating that this diagnosis had been missed. The danger to a particular patient receiving steroids may also vary according to his basic status. Intercurrent infection is more likely to develop in persons with a debilitating type of illness who receive steroids than in those with a milder illness or with a chronic illness such as rheumatic fever, in which debilitation is not a prominent factor.

Examples of the hazard of infection in patients receiving steroids are the 12 fatal cases of chickenpox in children reported by Haggerty and Eley.[10] The children were receiving steroids at the time of exposure to the disease.

From the experimental side it has been demonstrated that large doses of steroids definitely depress resistance to infections. This has been documented with experimental studies with bacterial, viral, fungal, protozoan, and even helminthic agents.[3b]

One would anticipate from the aforementioned statements that chemotherapeutic agents would counteract the adverse effect of the steroids. On the other hand, as shown in experimental animals, increasing the dose of steroids may overcome the effect of a given dose of a specific protective chemotherapeutic agent. This relationship is also limited by the toxicity of the particular substances. An example is the protective ability of penicillin in pneumococcic or group A beta hemolytic streptococcic infections in which this protection is diminished by the simultaneous administration of cortisone (Cortisone, Cortogen, Cortone). The effect of cortisone is overcome by increasing the dose of penicillin. However, it does not necessarily follow if tetracycline (Achromycin, Panmycin, Polycycline, Tetracyn, Tetracyn V) or chloramphenicol (Chloromycetin) is used instead of penicillin,[11] since the broad-spectrum agents are bacteriostatic generally and not bactericidal and the toxicity of these agents limits the increase in dosage.

Host resistance obviously also plays a role in determining the relative response to steroids and antibacterial agents. As shown by Johnson and Davey,[3a] relatively small amounts of streptomycin will overcome the effects of cortisone on tuberculosis in rats or rabbits in whom native resistance is relatively high; however, even with large doses of streptomycin, it is difficult to overcome all the adverse effects of cortisone on tuberculosis in guinea pigs. In essence then, the ability of specific agents to overcome the adverse effects of steroids in infection is a function of the host resistance and the virulence of the organism, as well as general characteristics of the drug.

Evaluation of clinical data on the relative effects of steroids and antibacterial agents is consistent with the points just made. The simultaneous administration of penicillin and cortisone to patients with pneumococcic pneumonia produced defervescence and symptomatic improvement more promptly than in those given penicillin alone. This was a carefully controlled study.[12] No adverse bacteriological results occurred, but renal insufficiency and prolonged hypothermia occurred in one patient treated with cortisone. Hypothermia has been reported by others[13] as a complication of cortisone therapy. This represents a situation in which the amount of penicillin used is adequate to overcome any possible reduction in host resistance induced by cortisone. We currently have a controlled study under way, comparing tetracycline and steroids.

Data have not been so favorable when infections have been studied in which specific treatment is more difficult. For example, in typhoid and brucellosis,[11] rapid defervescence follows the combined use of steroids and chemotherapy. However, no carefully controlled studies are available as there are with pneumococcic pneumonia, and one cannot be sure whether the improved response may not conceal an increased hazard. In a small series of patients acutely ill with brucellosis, prompt improvement occurred when cortisone was given for three or four days.[15] Apparently it was not harmful. Dubious results had been seen in patients with the more chronic stages of the disease.

A careful attitude was assumed early in the use of steroids in the management of patients with active tuberculosis. It was demonstrated experimentally that steroids suppress inflammation in the tissues but that tubercle bacilli multiply more rapidly. It is interesting, however, that there have been reported so few persons with spread of the disease while receiving steroids. Steroids do have a place in select cases of tuberculosis in conjunction with adequate chemotherapy. This seems to be particularly so in the more acute cases, as demonstrated by Johnson and colleagues[16] in a well-controlled study. They showed the rapidity with which patients with tuberculous meningitis improved and how promptly the abnormality of the spinal fluid could be corrected with the use of steroids. It has been suggested that the maximum period of therapy with steroids should be approximately three weeks. In this study, it was felt that the clearing of the fluid reflected the speed with which the exudative features of the disease could be reversed by steroids. It is well to bear in mind, however, that the number of controlled observations are few, and a rather marked improvement in management of tuberculosis in recent years makes it necessary to evaluate carefully whether the steroids have really contributed to the ultimate outcome.

Substantial symptomatic relief will usually occur when steroids are used with effective antibiotics. However, many infections, particularly those due to staphylococci and certain gram-negative bacteria, are difficult to manage with available agents. It is conceivable that the steroids in these situations may produce a more pronounced adverse effect because the agents are not as effective. These problems are under study, and currently no adequate clinical material is available for analysis. One is impressed by this need, despite claims for effectiveness of combined steroid-antibiotic therapy. Difficulties in evaluation have been noted by Lepper and Spies,[17] who studied these agents over a six-year period in over 1,000 persons. Although such agents are difficult to evaluate, they could not ascribe any marked benefits.

Antibacterial agents have been used as a prophylactic measure in patients receiving steroids. This is indeed a complex problem. Chemoprophylaxis generally has been effective when it has been used to eliminate susceptible micro-organisms such as group A beta hemolytic streptococci or meningococci, but it has not been particularly so when dealing with staphylococci or with gram-negative bacteria, particularly those which readily become drug-resistant. Prophylactic regimens will hardly be expected to confer adequate protection.

With the common antibiotic-resistant organisms, the feeling of security that the clinician may have in supposedly protecting the patient by chemoprophylaxis is hardly justified. It is particularly important that, when prophylactic chemotherapy is used, the dose of the agent is an adequate therapeutic one.

Available evidence strongly suggests that steroids, when given in sufficiently large amounts, do depress resistance to infections and that ability of antibiotic agents to overcome the disease despite the depressed resistance is limited. When the limitations are not in effect, the chemotherapeutic agents frequently do overcome the disease despite the depressed bodily resistance.

The experimental data may help us in understanding the use of steroids. The value of steroid hormones in adrenal insufficiency is well established. Studies by Finland and colleagues[2b] illustrate the response of the infected adrenalectomized mouse to cortisone. An uninfected adrenalectomized mouse was maintained well with 5 to 10 mcg. of cortisone daily. A dose of specific antiserum was selected which protected 50% of the nonadrenalectomized mice against approximately 50,000 virulent pneumococci. The same dose of antiserum protected 50% of the adrenalectomized mice against only about 1,000 pneumococci. With the administration of 25 mcg. of cortisone per day, resistance returned to nearly that of the intact animals. Doses of 25 to 100 mcg. of cortisone were almost optimal, but larger doses, such as 500 mcg., depressed resistance to a degree comparable to that produced by adrenalectomy. Thus, it would appear that infection places greater demand for steroids on the host. In addition, the optimal dose of steroid is critical, and an excess is likely to be harmful. Objective means for determining the optimal dose clinically are not yet available.

The evidence is questionable that adrenal insufficiency occurs as a consequence of severe sepsis, in the absence of preexisting adrenal cortical hypofunction (Addison's disease). Although direct effects of bacteria or the endotoxins on the adrenal cortex may lead to adrenal insufficiency, pretreatment with cortisone protects the adrenals from the damaging effects of, for example, diphtheria toxins but does not protect the animal from the lethal action of the toxin. It would appear that the damage caused by the toxin is so widespread that protection of the adrenal gland alone is of little benefit to the host. Recently it has been shown that endotoxins from gram-negative bacteria inhibit steroid genesis in the perfused adrenal gland.[18] Large amounts of endotoxin were used in this experiment, that is, large by in vivo standards. The possibility of direct damage to the adrenal as a cause of adrenal insufficiency cannot be discounted, despite the fact that the circulating corticosteroid levels in the animals given lethal doses of endotoxin were generally above the normal range.[19]

Of the clinical syndromes considered to be associated with adrenal insufficiency, none is more so than meningococcic toxemia with collapse, in which the use of steroid and related compounds is generally recommended as part of therapy. Controlled observations of the value of adrenal steroids in this situation are difficult to find. Since the introduction of steroids, a variety of them have been used, with varying degrees of enthusiasm. Although there is general agreement that the steroids should be given to patients with shock, there is apparently no definitive satisfactory evidence that a favorable response can be ascribed to the adrenal hormones. Failures have occurred after the use of such steroids,[17] and the collapse in this infection has been successfully corrected by treatment with levarterenol (Levophed), without corticosteroids.[20] Some authors emphasize the need for a pressor agent such as levarterenol to be administered along with the adrenal hormones and chemotherapy.[21] It is quite apparent that more information is needed concerning the value of the steroids in the management of meningococcic infection with shock.

All of us are aware that adrenal insufficiency may occur if infection appears in patients in whom exogenous steroids have suppressed steroid genesis. Under such circumstances, there is justification for increasing the dose of steroids. On the other hand, in patients who have received the steroids for a time but whose conditions have begun to deteriorate, this deterioration may be due to unrecognized infections. Increasing the dose of such agents under these circumstances is likely to aggravate the infection, unless specific chemotherapy is begun. The amount of steroid to be given to patients with relative adrenal insufficiency is still determined empirically. This is so, since determination of the level of circulating steroids in any instance may not necessarily reflect the rate of production or turnover in the host. Detailed study is required to answer this question. Adrenal insufficiency apparently may be a rare complication of severe sepsis. Relatively little objective support exists for the concept that adrenal insufficiency is common in severe infections and that the use of steroids is justified on that basis.

It has already been noted that the steroid levels are usually elevated in patients during severe infections. It is possible that, under certain circumstances, small doses of exogenous hormone might conceivably cause more steroid to enter tissue cells.

The protective effect of steroids against bacterial endotoxin depends on increased blood levels of steroids at the time of contact between endotoxin and susceptible tissues.[22] The protective action of cortisone is not demonstrable in toxemias due to exotoxins from Corynebacterium diphtheriae, Clostridium tetani, Cl. botulinum, Cl. perfringens, or Shigella dysenteriae.[2b]

Adrenal corticosteroids are effective in diminishing the inflammatory response, regardless of the stimulus. Dougherty[23] has analyzed the various stages of the inflammatory response in an attempt to determine at which level the corticosteroids influence the process. Existing evidence indicates that the primary focus of steroid action is on vascular responsivity. In general, the effects of steroids on inflammation and repair can be explained on the basis of their effect on vascular tone and permeability. The effects of corticosteroids on hypersensitivity reactions and similar tissue responses to immunologically active stimuli probably reflect the general anti-inflammatory effect of these steroids rather than a specific effect on purely immunological mechanisms.

At present, it is generally agreed that steroids depress antibody production but do not alter the degradation rate of the preformed antibodies.[24] The mechanism by which this happens is not quite clear. There may be several ways in which this occurs. For example, the antigen may be held locally, due to a vascular effect of the steroids. The antibody-forming mechanism may be directly depressed, or the relationship with the antibody-forming cells to the intermediary cells in the process of antibody production may be altered.

As far as the steroids and particularly the reticuloendothelial function are concerned, from available evidence, it would seem that this function is disturbed by administration of the steroids and that this disturbance is manifested less in the initial response of the reticular cells to an injected load than in the capacity of these cells to recover their function after such a load has been administered.[25]

In conclusion, it is quite obvious that the exact status of steroids in the collateral management of infections is still not definitive and requires much in the way of further controlled clinical study.

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FROM THE ATOM TO THE PATIENT

GUEST EDITORIAL

Irving S. Wright, M.D.

IT IS presently fashionable in scientific circles to regard basic research as the high-priestess of the new era, and certainly no one can challenge this general position. However, the definition as to what basic research really consists of and who is doing it varies, depending on the spokesman. In the medical field the pathologists, the biochemists, and the anatomists consider themselves to be the basic scientists. But in broader scientific circles the physical chemists, the physicists, and the mathematicians, with the many ancillary branches of these disciplines, are not unanimous in accepting the biochemists or the pathologists into their fold as true basic scientists. Even within the medical field, it seems to make a difference whether the investigator works with an electronic computer, test tubes, mice, guinea pigs, or human beings—the implication in some quarters being that man working with man as his subject is in some way a lesser scientist. This "caste" system tends to compartmentalize groups of workers and hampers the close cooperation between all types of scientists which is necessary if we are to benefit maximally from our increasing investment in research.

At every level science is the search for new facts, and a fact discovered while investigating man may be just as important as one disclosed by using a cloud chamber and a cyclotron. A fact unearthed in a physicist's laboratory may prove to be of great importance, but the mere site of discovery does not guarantee that it will ever be of value to mankind. By the same token, an observation made on a normal person in a physiology laboratory or on a patient in the ward either may have little significance or may lead to the saving of countless lives. It is not where the discovery is made or who makes it which determines its value.

Scientists should stop categorizing research as basic versus applied or clinical; instead they should consider any new finding on the basis of its value to man. This is not to imply that an important discovery must relate directly and immediately to man's health, comfort, or pleasure; but to be of greatest worth it should in some way ultimately contribute to the well-being of mankind. The remote effects of a new observation cannot always be foretold, but acclaim should await the verdict of time. Eugene Dubois once said to me: "The discovery *of a physiological response to stimulation or* the development of a new drug may be easy or even accidental. Its evaluation is apt to be much more difficult." Hence the task for developmental or applied research may require just as critical scientific acumen as that needed for the early observations.

Science for science's sake is not good enough; it is a limited credo. Overemphasis on this philosophy seems to have brought us to the brink of a catastrophe from which escape is possible only by a miracle more remarkable than the atomic bomb. This miracle must be of the spirit and will not evolve from the laboratory. We are in a quagmire from which there is no easy escape, but it may help if, in the future, more scientists ask themselves whether their work has any potential value to the human race.

Research is progressing at breakneck speed in a thousand unrelated and uncoordinated directions. New knowledge, some important, some of seemingly less significance, is being recorded and developed at a rate never dreamed of even 20 years ago. Yet, of what benefit is a basic discovery if it remains unrecognized and unused? Here the new science of more rapid communication with its many facets should have full play.

In summarizing, it is believed to be unwise to rate scientists on different levels because of the particular technique which they use. More thought should be given to the value of research as it applies to the human race than has been the case in some quarters in the past. Discoveries which are made but not disseminated and applied are of little significance so long as they remain unknown to others. Rapid dissemination of knowledge regarding new findings is one of the major challenges of medical investigators and those interested in the various techniques of communication.

From New York Hospital, New York.

ORGANIZATION SECTION

ADDRESS OF PRESIDENT GUNNAR GUNDERSEN BEFORE THE HOUSE OF DELEGATES

In scores of ways the past year has been an exciting one for our Association—and consequently for me. To relate them all would require a speech lasting many hours. In the next few minutes allow me to make some observations and suggestions without delving into too many issues or accomplishments.

Blue Shield and the Aged

I will begin by saying that it has been a personal thrill to witness the revolutionary developments in the field of health insurance coverage for our senior citizens. Last December when American medicine declared its intentions to develop, by voluntary means, programs of health care coverage suitable to the needs of the aged, the response of Blue Shield plans throughout the country was indeed gratifying. These plans unhesitatingly committed themselves to the task of implementing the A. M. A. action calling for the development of low-cost medical care coverage for the aged. Immediately after our Minneapolis meeting, the National Association of Blue Shield Plans issued a nationwide press release announcing that each of the 64 Blue Shield Plans in the country had been instructed to go to work immediately with their local sponsoring medical societies to draft benefit schedules and rates for coverage that local doctors felt necessary to meet the needs of persons past 65.

Local plans lost no time in translating these instructions into action. In little more than a month the first Blue Shield programs for the aged began to take shape under local medical society guidance. Among the first plans with such programs were those in Iowa, Connecticut, California, Nebraska, and Wisconsin—to identify a few.

Thus, Blue Shield has provided an inspiring demonstration of its desire to be among the first to serve the aims of medicine in extending voluntary forms of health care into new and important areas of public need. For this, these plans deserve a vote of confidence from the profession at large and from each of their local sponsoring medical societies.

Our new Committee on Insurance and Prepayment Plans also is expanding our working liaison between all insurance groups via the mechanism of the Health Insurance Council. Through this Committee's activity I am confident we—the medical profession and the voluntary health insurance industry—can do a better over-all job.

As many of you know, it has been my conviction that "as medicine goes . . . so goes voluntary health insurance." And I might add that this could just as easily be turned around and be equally appropriate. I use this adaptation of an old familiar slogan with this idea in mind: Neither of us can go it alone. Neither of us can secure our own position without the assistance of the other. Indeed, neither of us can survive separately.

Therefore, I believe it should be apparent to all physicians that one of medicine's most important challenges—now and in the future—is to adhere to the principle of charging for professional services on a basis that permits the insurance industry to sell health insurance at a price that people can afford to pay.

If this is not done, obviously the insurance industry cannot continue with forward-looking, creative planning in voluntary health insurance coverage. And the end-result will be the assumption by the federal government of the tasks now performed by the medicine-insurance partnership.

Keeping Abreast Medically

While we follow the principle of making our professional fees reasonable for the services rendered, we also are duty-bound to see that these services are of the highest quality. I feel that our Association for many, many years has sought actively to improve the quality of medical care. We have pushed for high standards in medical education, hospital accreditation, licensure, and specialty training.

Our state and local societies, too, are employing a great many devices to assure the public of high quality of medical care. Physicians themselves are making sincere and dedicated efforts to keep abreast of the rapid developments and progress in medicine. This they are doing by participating in various programs of continuing medical education. There is no doubt that this individual and group action to maintain and better the quality of medical care has been an important factor in making American medicine the finest anywhere in the world.

I see no necessity for a "crash" program on the part of physicians to improve the quality of medical care. Throughout our country medical care generally is excellent. However, because of the current unmatched progress in medical science

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Read before the 108th Annual Meeting of the American Medical Association, Atlantic City, June 8, 1959.

there must be an awareness and a willingness on the part of every physician that the need to keep abreast of medical advancements is his personal responsibility—to his patient, to himself, and to American medicine.

To be prepared for any medical situation we must do our "homework." We must be ready to deliver "1959 medicine"—intelligently and with skill. Anything less, such as 10-year-old or 5-year-old medicine, will not do. Patients do not want 1949 or 1954 medical care. They desire up-to-the-minute medicine and they should get it. Any physician who is not making an effort to keep abreast of medical knowledge blackens the eye of American medicine just as much as the person who overcharges.

I say this to you, with all the sincerity at my command, that if all the words I have spoken and written in the last year are forgotten but the two words "keep abreast" are remembered, I will have considered my term of office a success.

Through our scientific journals, scientific meetings, our work on postgraduate and refresher courses, medical motion pictures, the lending library, and scores of other mechanisms, the American Medical Association strives daily to help its members stay on top of new things in medicine. To further our Association's influence in the scientific field we have invited 15 of the nation's top scientists to take an objective look at the present and future scientific activities of the A. M. A.

These scientists will make up an *ad hoc* advisory committee on scientific activities. They will advise the A. M. A. which scientific activities should be continued, which ones should be dropped, and what new activities should be undertaken. Better ways to coordinate the A. M. A.'s scientific activities also will be considered. This committee is another example of our continuing efforts to get the greatest mileage out of our Association's work to assist us all in having the latest and best information available.

Food Faddism

Our endeavors to keep the public informed on sound health have been equally constant and effective. As an example, I point with pride to the past year's campaign against food faddism and for proper nutrition. Cooperating closely with the Food and Drug Administration, the National Better Business Bureau, and state and county medical societies, the Council on Foods and Nutrition carried out a dramatic program of public education on food quackery and on correct diets and dieting. More than 2,000 club and television audiences saw our film, "The Medicine Man." Thousands of persons saw our exhibit, "Nutrition Nonsense and Food Quackery." A half-million copies of our pamphlet, "The Healthy Way to Weigh Less," were distributed. And 6,000 comprehensive kits containing further data on these subjects were used through the cooperative efforts of medical societies.

This whole campaign has brought our Association national commentary in all mediums and has resulted in high and wide commendation. For their cooperative work in this project I want to give special praise to the Food and Drug Administration and the National Better Business Bureau. Here again is vivid evidence of the fruits of close liaison with groups interested in getting across to the public a sound and factual message regarding the health and the pocketbook of the American people. The job has been done well, and I salute these two organizations and all our medical societies for their splendid cooperation.

A. M. A. Reorganization

As you well know, our Association has been reorganized from top to bottom and from stem to stern. This has been done to make the A. M. A. more effective in professional and public matters. As your President, I have seen this reorganization take place and take shape. It has not been a hit-or-miss proposition. It has had some short-range goals in mind, of course, but essentially it has been aimed at the long-range purposes of a united, alert, and dynamic organization that will serve all the profession and all the people of this country.

I am proud to have served you as A. M. A. President during this time. I am even more proud of the positive strides being made by our headquarters' staff under the direction and leadership of Dr. F. J. L. (Bing) Blasingame, our Executive Vice-president.

In my opinion he has acted with foresight and courage and has built a staff that has depth and proved ability in their respective fields. Together they are making the medical profession and public fully aware of the solid, enlightened job our Association is doing on scores of medical fronts—whether they be scientific, educational, or socioeconomic.

I am in firm agreement with Dr. Blasingame that our Association has the size, the stature, the experience, and the resources to lead and guide our nation's health team in the various fields of activity. And I believe with him that medicine never was stronger in its ability to serve and to meet human needs.

There is no doubt that medicine is destined to be a vital part of the texture of the future American society. I believe that today our Association is better prepared to serve both the public and the profession than at any other time in its history.

Now in closing out my stewardship my heart tells me to offer you gentlemen of the House of Delegates my warm thanks for selecting me as your A. M. A. spokesman for the past year and my sincere appreciation to each of you for your unstinting support—especially when it was sorely needed.

Robert Browning wrote these lines in his poem "Rabbi Ben Ezra": "Grow old along with me. The best is yet to be." Gentlemen, after serving you and this Association for the past two years as President-elect and President, I say to you that Browning's admonition does not apply to me. I have had the best. What is "yet to be" can never compare with the experiences I have enjoyed.

ADDRESS OF PRESIDENT-ELECT LOUIS M. ORR BEFORE THE HOUSE OF DELEGATES

In my brief remarks this morning, I shall look at a few issues and challenges which I believe should have close attention from this House of Delegates and the entire medical profession—not just for the next 12 months, but for years to come.

The policy actions taken at this meeting will be vitally important to American medicine. In addition, we must give constant attention to many other problems—old ones, new ones, and hardy perennials. Taking the long-range view, let me point out four particular problem areas which demand full recognition and advance planning to meet the needs of the future.

Costs of Medical Care

One of these is the cost of medical care. Numerous federal agencies and state governments are conducting studies of hospital costs, health insurance programs, and other economic aspects of medical care. Everyone is writing or speaking on this subject—politicians, economists, magazine writers, newspaper columnists, and curbstone experts, who sometimes air their views through the press.

The American public, and rightfully so, has an intense interest in the costs of medical care. Those costs involve the people's lives, health, and pocketbooks. But the mass of written and spoken words frequently produces confusion and misinterpretation of facts in the field of medical economics. Quick and easy information—sometimes misinformation—is coming from persons who may be adept at statistics but who lack a thorough knowledge of all the medical and human elements that go into health care.

Therefore, I strongly urge that the American Medical Association take the lead in providing authoritative information gathered by qualified personnel with a real understanding of all the economic, medical, and human factors involved in this complex subject.

As I see it, such a program should involve much more than the collection of dry statistics; it should include continuing, simplified interpretation, made understandable to the public. It should include studies of all possible ways to stabilize or reduce the costs of medical care, hospitalization, and health insurance. It should encourage the development and increased use of rest homes, nursing homes, rehabilitation centers, chronic illness facilities, home-care programs, homemaker services, and other special facilities for patients who do not need complete hospital care.

Finally, in the field of hospital costs—and this perhaps is the major problem in the over-all picture—the A. M. A. should draw attention to all new ideas on the organization, design, and construction of hospitals. One of these is the concept known as "progressive patient care," which means the systematic classification of patients according to their medical needs.

Under such a program the hospital can concentrate expensive equipment and highly skilled personnel in an intensive care unit for patients who need close attention. Then, as a patient improves, he can be moved to an intermediate care unit and finally to a convalescent or self-help unit. This could represent the concept of automation in patient care. This concept improves patient care and produces economy in both construction and operating costs. In the field of "atomedics" we are going to see bricks and mortar, metal and plaster being replaced by plastics. Adhesives will be substituted for nails and bolts. We will also see the increasing usage of computing devices, all of which will assist in reducing costs. Moreover, because of the variation in room rates for the different units, the hotel aspects of hospitalization can be reduced.

In short, all fresh, imaginative approaches should be explored by the A. M. A. in a vigorous, continuing study of medical and hospital costs.

Need for Dedicated Young People

The second area which I have in mind is the recruitment of qualified, dedicated young people to enter the study of medicine. For the past 30 years or more the production of new physicians by our medical schools has kept pace with the nation's growth in population. However, we no longer can relax in the complacency of past or present accomplishments. We are entering a period when increasingly rapid population growth, plus the mounting number and complexity of medical services, will require a still greater increase in the annual number of medical school graduates.

Last December in Minneapolis this House of Delegates approved a clear, positive statement urging the sound expansion of existing medical schools and the creation of new medical schools by universities which can provide the proper academic and clinical setting. This program of expansion would be based on a careful, continuing study of the changing needs in all categories of medical activity.

Read before the 108th Annual Meeting of the American Medical Association, Atlantic City, June 8, 1959.

We accept the need for a greater quantity of medical service in the future. At the same time we are encouraging the medical schools to experiment in new programs to even further improve the quality and content of their curriculums.

There is one more very important consideration relating to applicants—the mental, moral, and ethical caliber of tomorrow's doctors. It will not be enough to have a larger number of well-trained physicians in the years ahead. They must also be dedicated men and women with a profound, sincere realization of their obligations to their patients and to all of humanity.

With these ideas in mind, I strongly urge the medical profession to consider the development of a planned, organized program to recruit the best-qualified young people into the study of medicine. Such a program, to be effective, must be carried out on all levels—national, state, local, and individual.

The A. M. A. already is engaged in a variety of efforts along these lines. It participates each year in the National Science Fair. It is producing a new career guidance film on medicine. It provides informational materials for interested young people. The A. M. A., however, cannot do the job alone. It must be carried down to every local community.

Basically, this is a grass-roots responsibility which should be assumed by every individual physician. He should take the time to talk medicine with promising young people of high school and college age. In particular, he should concentrate on those who have not only scientific aptitudes but also the capacity for dedicated service.

Medical Research

The third area to which I would call your attention is that of research. It has been estimated that by 1970 this country will be spending about 1 billion dollars a year on medical research, with about one-half of that total coming from private philanthropy and industry. We in the medical profession must exert influence and leadership in seeing that research funds are spent wisely, not just in the economic sense but also from the standpoint of scientific principles and the public interest.

Medical research in the years ahead will require more and more money and facilities. It will require increasingly intensive efforts to recruit and train medical scientists with an aptitude for research. It also will require constant vigilance to maintain a sound balance between practical, applied research and basic, long-range research. The A. M. A. should encourage, in all areas, the creation of "life-time grants" in basic research. It is only in this way that we will be able to attract dedicated minds to pursue basic research with complete freedom from worry and distractions, financial and otherwise.

Those of us in active practice are, quite naturally, interested in the practical results of medical research—the new drugs, treatments, and techniques which we can apply in our everyday work. However, we must never forget that the vaccines, antibiotics, and hormones in use today are only the end-results of basic discoveries made years ago in such fields as pathology, bacteriology, and biochemistry.

Everyone, in and out of medicine, hopes and prays that a cure will be found for cancer. However, if and when we achieve an ultimate, complete conquest of cancer, it probably will come through new, basic knowledge of body cells—how and why they behave as they do. This kind of research will then provide specific clues for the development of new methods of treatment and prevention.

The basic research of today produces the lifesaving drugs, preventive vaccines, and dramatic surgical techniques of tomorrow. As Dr. Hans Selye has pointed out, the nation's culture, health, and strength depend primarily on its creative basic scientists—those whose main endeavor is to search for the kind of truth that can be verified by experience.

And so, whether we are promoting private research programs or expressing our opinions on legislation involving medical research funds, let us fight always for proper recognition of those dedicated men whose basic research may have a profound effect on the future of mankind.

Responsibilities in Aging

The fourth and final subject I have in mind is aging and health care of the aged. As you know, this involves a complexity of problems with both immediate and long-range aspects. The A. M. A., on the national level, is working hard on an expanding program to bring about a sound, realistic approach to all phases of these problems.

But here, again, the A. M. A. cannot do the job alone. I strongly appeal to every state medical society, every county medical society, and every physician to accept a share of the responsibility in carrying out the national program. I charge every member of this House of Delegates to review the work in his state and to help stimulate even greater activity.

This responsibility must be met through medical leadership. If it is not, the politicians will take over the field. Every individual doctor must recognize the problems that exist in the field of aging. The key to sound solutions lies in community planning to develop services and facilities attuned to the needs of older people. This will require close cooperation among physicians, hospitals, and all other interested groups.

Encouraging progress has been made during the past six months by medical societies, prepayment plans, and insurance companies to meet the health insurance needs of senior citizens. However, we probably have less than a year in which to demonstrate—dramatically and convincingly—that private health insurance can do this particular job. I appeal for an accelerated, snowballing program which will demonstrate medicine's leadership and wisdom in meeting the problems of an aging population.

Medical Statesmanship

Finally, a word on something which I consider of paramount importance, many issues coming before you at this meeting contain the seeds of controversy. They involve subjects on which physicians have a wide range of opinions.

I urge every interested physician to express himself fully at the reference committee open hearings tomorrow. I urge every delegate to make full use of his privileges on the floor of this House. At the same time, I hope that all discussion will be based on a maximum of reason and logic. Above all, I hope that medical statesmanship will prevail—keeping in mind not only the interests and standards of medicine but also the medical and economic welfare of the people whom we serve.

REGISTRATION AT THE ATLANTIC CITY MEETING

Registration Count, by State, June 6-10, 1955

Alabama	56	Nebraska	38
Alaska	1	Nevada	8
Arizona	24	New Hampshire	26
Arkansas	24	Atlantic City, N. J.	174
California	380	New Jersey	1,715
Colorado	58	New Mexico	19
Connecticut	202	New York	2,054
Delaware	132	North Carolina	107
D. C.	271	North Dakota	13
Florida	143	Ohio	414
Georgia	74	Oklahoma	32
Hawaii	17	Oregon	24
Idaho	7	Pennsylvania	2,491
Illinois	394	Puerto Rico	7
Indiana	119	Rhode Island	71
Iowa	62	South Carolina	39
Isthmian C. Z.	0	South Dakota	15
Kansas	36	Tennessee	75
Kentucky	77	Texas	192
Louisiana	52	Utah	13
Maine	23	Vermont	19
Maryland	397	Virgin Islands	0
Massachusetts	272	Virginia	216
Michigan	214	Washington	62
Minnesota	123	West Virginia	78
Mississippi	19	Wisconsin	71
Missouri	106	Wyoming	8
Montana	12		
		Total	11,309

Registration Count, by State, June 7-12, 1959

Alabama	44	Nebraska	31
Alaska	5	Nevada	6
Arizona	30	New Hampshire	23
Arkansas	21	Atlantic City, N. J.	96
California	393	New Jersey	1,819
Colorado	54	New Mexico	20
Connecticut	184	New York	2,047
Delaware	142	North Carolina	124
D. C.	313	North Dakota	20
Florida	213	Ohio	409
Georgia	88	Oklahoma	43
Hawaii	20	Oregon	33
Idaho	8	Pennsylvania	2,742
Illinois	438	Puerto Rico	20
Indiana	136	Rhode Island	60
Iowa	60	South Carolina	27
Isthmian C. Z.	3	South Dakota	10
Kansas	55	Tennessee	86
Kentucky	77	Texas	202
Louisiana	82	Utah	22
Maine	20	Vermont	15
Maryland	406	Virgin Islands	1
Massachusetts	303	Virginia	129
Michigan	204	Washington	69
Minnesota	110	West Virginia	75
Mississippi	24	Wisconsin	89
Missouri	112	Wyoming	11
Montana	9		
		Total	11,816

Registration by Section, June 6-10, 1955

Anesthesiology	295	Pathology & Physiology	317
Dermatology & Syphilology	319	Pediatrics	508
Diseases of the Chest	293	Physical Medicine & Rehabilitation	124
Experimental Medicine & Therapeutics	78	Preventive & Industrial Medicine & Public Health	321
Gastroenterology & Proctology	271	Radiology	372
General Practice	2,158	Surgery, General & Abdominal	1,316
Internal Medicine	1,975	Urology	207
Laryngology, Otology & Rhinology	301	Session on Allergy	67
Military Medicine	132	Session on Legal Medicine	9
Nervous & Mental Diseases	305	No section checked	630
Obstetrics & Gynecology	638	More than one section	45
	536		
	329	Grand total	11,546

Registration by Section, June 8-12, 1959

Anesthesiology	317	Pathology & Physiology	294
Dermatology	340	Pediatrics	414
Diseases of the Chest	401	Physical Medicine	126
Experimental Medicine & Therapeutics	142	Preventive Medicine	206
Gastroenterology & Proctology	251	Radiology	359
General Practice	2,049	Surgery, General & Abdominal	1,201
Internal Medicine	1,862	Urology	189
Laryngology, Otology & Rhinology	276	Session on Aging	42
Military Medicine	119	Session on Allergy	65
Nervous & Mental Diseases	424	Session on Cosmetic Surgery	14
Obstetrics & Gynecology	539	No section checked	1,135
Ophthalmology	541	More than one section	380
Orthopedic Surgery	303	Grand total	11,989

Registration, Other Countries, June 6-10, 1955

Africa	4	Israel	1
Argentina	7	Italy	3
Australia	5	Japan	2
Austria	1	Korea	6
Bolivia	3	Lebanon	1
Brazil	6	Mexico	2
Canada	63	Pakistan	2
Chile	7	Peru	3
Colombia	4	Philippine Islands	10
Cuba	19	Portugal	1
Denmark	2	Scotland	1
Dominican Republic	1	South Africa	4
Ecuador	1	South America	4
Egypt	4	Spain	2
England	14	Sweden	4
Finland	1	Switzerland	3
Formosa	4	Syria	1
France	4	Thailand	3
Germany	7	Turkey	2
Greece	1	Venezuela	4
Holland	3	Yugoslavia	1
Iceland	1		
India	9	Total	237
Indonesia	2		11,309
Iran	3		
Ireland	1	Grand total	11,546

Registration, Other Countries, June 7-12, 1959

Africa	1	Israel	2
Argentina	7	Japan	6
Australia	1	Korea	2
Austria	3	Lebanon	1
Brazil	13	Mexico	8
Canada	60	Netherlands	2
Chile	1	New Zealand	1
China	1	Peru	2
Colombia	1	Philippine Islands	4
Cuba	12	Spain	1
Ecuador	3	Sweden	2
Egypt	1	Switzerland	5
El Salvador	1	Thailand	2
England	7	Turkey	2
France	2	Uruguay	2
Germany	6	Venezuela	3
Guatemala	2		
Haiti	1	Total	173
Honduras	2		11,816
India	2		
Iraq	1	Grand total	11,989

THE 1959 SCIENTIFIC ASSEMBLY

Many unusual features highlighted the 108th Annual Meeting at Atlantic City. The number of sections participating in various symposiums was increased, and new topics which hitherto had been considered only in individual papers were approached at the symposium level. A symposium on the management of childbirth brought together seven sections, and six sections met at a symposium on hepatic diseases.

Seven of the 21 scientific sections observed 100th anniversaries. Some of these were distinguished by special guest speakers who gave centennial addresses. The Section on Experimental Medicine and Therapeutics heard J. N. Morris, of London, present a follow-up summary of earlier studies relating to occupation and heart disease. A commemorative luncheon of the Section on Obstetrics and Gynecology was addressed by Andrew Claye, of Leeds, England, president of the Royal College of Obstetricians and Gynecologists. R. R. A. Coombs, of Cambridge, England, spoke on the demonstration of antigens in tissue cells by mixed agglutination reactions, at a meeting of the Section on Pathology and Physiology. Walter L. Bierring was guest speaker of the Section on Preventive Medicine, his address dealing with the changing concepts of that specialty over the period 1859 to 1959. A similar 100-year survey was presented by John H. Mulholland in his chairman's address to the Section on Surgery, General and Abdominal. Other sections marking centennials were Internal Medicine and Nervous and Mental Diseases.

Because of the multiplicity and overlapping of some outstanding scientific presentations physicians found it necessary to follow a tight schedule in attending the various discussions, and sometimes priorities had to be sacrificed to superpriorities. Many of these papers will be published in THE JOURNAL or one of the A. M. A. specialty journals.

The 385 scientific exhibits claimed and merited detailed attention from the 13,143 physicians, residents, and interns who registered for the meeting. The usual wide variety of presentations was assembled, with many new concepts and techniques available for evaluation. Attracting perhaps the greatest audience were the special features that have become annual presentations. Fresh tissue pathology demonstrations were given to a never-ending line; the annual physical examination service for physicians was more crowded than ever; demonstrations of fracture treatment techniques had their usual quota of visitors; and the special diabetes exhibits and conferences provided useful practical guidance for many physicians with unusual treatment problems. Other special features included pulmonary function testing, the Student American Medical Association (S. A. M. A.), the history of medicine, science fair exhibits, arthritis and rheumatism, and diet conferences provided by the A. M. A. Council on Foods and Nutrition.

Hospital Sepsis Problem

Although there is rarely enough concentration on one specific medical problem to permit its identification as a convention "theme," it should be noted that the current concern over hospital sepsis found expression at virtually all levels. An exhibit prepared by the University of Texas Medical Branch detailed a control program developed to cope with an outbreak of staphylococcic infection in a nursery for newborn infants. Prolonged continuous screening of all personnel in the obstetric and nursery areas established the importance of the upper respiratory tract as a reservoir for these organisms. Another exhibit dealing with the epidemiology and control of hospital staphylococcic infections, prepared by the US Public Health Service, traced pathways of infection in both hospital and community and demonstrated control measures. J. T. Godwin, one of the members of this exhibition team, described to a session of the Section on Surgery, General and Abdominal, an outbreak of staphylococcic infection that was traced to a member of the surgical team carrying bacteriophage strains 80-81 and 80-81-52-52A.

In a premiere showing to an overflow audience Wednesday evening a new 30-minute sound and color film, "Hospital Sepsis—A Communicable Disease," stressed the world-wide problem of cross infections. Prepared under the supervision of a committee representing the A. M. A., the American College of Surgeons, and the American Hospital Association the film provides valuable educational material for all levels of hospital personnel. It can be obtained on loan from the A. M. A. Department of Motion Pictures and Medical Television, Mr. Ralph Creer, Director, after Aug. 1. On Thursday morning a color television panel program dealing with the staphylococcic problem, with William A. Altemeier as chairman and Stuart Mudd, William Sandusky, and T. C. Schaeffer as participants, presented the concept that three basic sources are responsible for such infections: patients, personnel, and physical environment. Emphasis was placed on the value of simple asepsis routines that could be followed faithfully, rather than on any "crash" program. Misuse of antibiotics was mentioned as a possible factor in some situations. Although maternity and pediatric departments appear most vulnerable so far as hospital epidemics are concerned, it was pointed out that virtually all patients are likely candidates for infection because of their presumed subnormal condition. Reservations were expressed regarding the usefulness of immunization through use of specific bacterial vaccines. A survey of several hundred hospital epidemics has revealed that Staphylococcus aureus, coagulase-positive strain, bacteriophage type 80-81 is the chief offender.

Finally, a motion picture prepared by H. Rocke Robertson, Vancouver, B. C., also presented on Thursday morning, illustrated the various types of staphylococcic infections encountered in surgical patients and breaks in technique that may lead to surgical wound infection. It emphasized, as did the color film mentioned, that patients, especially those with furuncles or more extensive skin infections, are the most common original source of an infection which often spreads through the immediate hospital area with incredible speed.

Useful orientation regarding radiation problems was provided by a film, "Radiation Hazards and Control in Diagnostic Radiology," prepared under the supervision of the American College of Radiology. Introduced by Wendell G. Scott for its premiere showing at the general scientific meeting Tuesday morning, it was described by R. L. Chamberlain, commentator, as a documentary film intended to define the status of knowledge about x-ray effects and how such knowledge can be applied to treatment problems. Its sensible, matter-of-fact approach suggests that this film should find widespread usefulness. In the scientific Section on Radiology an exhibit on radiation, identified as a "growing health problem," defined radiation and described its biological effects. New sources of radiation were listed, with data on efforts being made to keep exposures to a minimum. It indicated that exposures incident to medical x-ray studies can be effectively reduced without loss of diagnostic quality.

Useful clinical data on iron metabolism were provided by Carl V. Moore, recipient of the 1959 Joseph Goldberger Award in Clinical Nutrition, in his lecture marking this occasion. According to Moore, reduction in the incidence of iron deficiency constitutes a medical and public health challenge of world-wide importance. In some countries the hypochromic anemia produced by iron deficiency becomes so severe that it is a direct or important contributory cause of death. The anemia more commonly exacts its toll by causing moderate to advanced degrees of fatigue, a decreased sense of well-being, lessened work efficiency, and a staggering sum total of ill health. Within any population group the frequency of iron deficiency is greatest among infants, children, and young women during the childbearing years. There is no practical way to eliminate iron deficiency, for the reason that, in biological terms, hemoglobin contains a large amount of iron; as long as people have diseases which cause them to bleed, loss of iron will often be greater than can be compensated for by a reasonable diet. Significant reduction in the incidence should, however, be possible.

Moore believes physicians should be more sensitive to the importance of minor chronic bleeding, more alert to detect increased menstrual loss, and more conscious of the iron demands of normal growth or pregnancy. In most instances, he said, dietary adjustments or iron supplements—not full therapeutic doses of iron—would be adequate to restore a positive iron balance. When one deals with prevention and not therapy he is usually concerned with a situation in which 2 to 3 mg. of additional retained iron per day represents the difference between a positive and a negative balance. There has been reluctance to recommend iron supplements for fear the practice might be abused, but if supplementation were limited to those periods of demonstrated increased needs, much could be accomplished.

A significant point made by Moore was that, during the past two decades, blood donation has become a frequent type of "hemorrhage"; in the United States alone more than 5 million pints of blood are collected yearly. Dr. Moore expressed as his personal conviction the belief that failure to provide iron supplementation to blood donors is no longer excusable, although he recognized possible deterring factors such as criticism of blood bank directors by the medical profession for engaging in "mass therapy," or fear that prospective donors may be discouraged by the implication that giving blood might be harmful to them.

General Scientific Meetings

Other activities at the general scientific meetings on Monday and on Tuesday morning included a symposium on leukemia, with papers on research, treatment, and immunohematology. Highlights of the former included emphasis on the need for increased research activity and the changing pattern of complications of leukemia. It was pointed out that pseudomonal and clostridial infections are on the increase in such patients, with septicemia being seen more commonly, and that both bone and central nervous system involvements are also showing a higher incidence rate. The latter appears most frequently when the white blood cell count is in the range of 300,000 per cubic millimeter and there is direct involvement of the brain itself. In treatment, withholding of therapy may often be as useful as embarking on a routine before the patient's status has been completely evaluated; no treatment should be determined on the basis of white blood cell totals alone.

In what was described as a new experiment, for the first time six sections gathered in the convention hall ballroom for a symposium on hepatic disease. These included Experimental Medicine and Therapeutics, Gastroenterology and Proctology, General Practice, Internal Medicine, Pathology and Physiology, and Radiology. A wide coverage of hepatic disease was provided, including discussions on conjugation and excretion of bilirubin, hepatic coma, viral hepatitis, effective use of radiology in diagnosis of hepatic disease, and newer concepts of cirrhosis. The speaker on the last topic limited his discussion to the role of alcohol, considered the most common factor in the production of cirrhosis. He pointed out that there is considerable difference in susceptibility among individuals, and, as was already known, that dietary errors or omissions probably play a significant contributing part in many instances.

Another overflow audience heard a symposium on hypnosis, at which much-needed facts received appropriate emphasis. A joint meeting of the sections on Anesthesiology and Nervous and Mental Diseases, this included discussions of the basic concept of *hypnosis, techniques,* and *applications* and misapplications. Harold Rosen, Chairman, Committee on Hypnosis, A. M. A. Council on Mental Health, pointed out that the danger of hypnosis lies not in its use as such but in failure to appreciate its many limitations and to make proper selection of patients in whom it can be used satisfactorily. Any physician can be taught the technique in a short time and there is no need of any special apparatus for induction of hypnosis, Rosen emphasized. He criticized specifically the postulation that alteration of brain wave rhythm by any machine will induce the hypnotic state, and declared that it can do no more than possibly induce sleep. Instances of the danger of making use of hypnosis casually and without proper evaluation of the patient were cited. This modality is of no value if the patient must have some outlet for suppressed emotions and may even be dangerous. All too often patients seeking hypnosis treatment may present complaints that are masking some severe underlying psychosis. The general conclusion appears to be that hypnosis is something that the average physician is not likely to find applicable in daily practice. However, use of hypnosis in inducing anesthetic states offers good possibilities, it was pointed out in a presentation on hypnoanalgesia and hypnoanesthesia for cardiac surgery, presented by M. J. Marmer. Other papers delivered at this symposium included a discussion of addicting drugs and the anesthesiologist, by E. R. Bloomquist, and a study of cardiovascular response to transcranial electric stimulation, by D. J. Richardson and co-workers.

The large-scale symposium on progress in the management of childbirth brought together the sections on Anesthesiology, Diseases of the Chest, General Practice, Nervous and Mental Diseases, Obstetrics and Gynecology, Pediatrics, and Preventive Medicine. Meeting in the convention hall ballroom this session was made up of a three-part presentation. The first dealt with the prenatal period; papers were heard on general medical services, nutritional aspects, a study of maternal diaphragmatic breathing function, and nervous and mental considerations. The second part, devoted to the natal period, included papers on obstetric anesthesiology, care of the patient with heart disease during pregnancy and at childbirth, management of labor and delivery, and protection of the fetus. In the third section general aspects of the postnatal period were considered, with special attention to cerebral problems and resuscitation in the newborn infant.

Tying in with this symposium was the exhibit of the Committee on Maternal and Child Care, A. M. A. *Council on Medical Service, dealing with* perinatal mortality and morbidity. In this graphic presentation statistics on maternal, neonatal (under 28 days), postnatal (28 days to under 1 year), and infant (under 2 years) mortality were updated to cover the 10-year period 1948-1957. In all these there was a slowing of the percentage rate of decrease, as would be expected in comparison with the preceding 10 years, but nevertheless ample evidence was presented that significant progress is still being made. The "Guide to Maternal Death Studies," prepared by the Committee with assistance from nine groups active in this general area, was described as being available to state and local medical societies, health departments, and hospitals with obstetric departments and nurseries for newborn infants. Other assistance available from the Committee includes consultation and speaker service, loan kits of pertinent material, and sponsorship of educational meetings. Illustrating the extent of the problem was a chart placing the death total during the first seven days of life at 70,000 a year, with an additional total of 70,000 fetal deaths from the 20th week of gestation. A conservative total of 60,000 was assigned to morbidity factors including such neuropsychiatric disabilities as cerebral palsy, epilepsy, and mental retardation, and other congenital defects.

Disease Among Aged

Interesting material on new concepts was provided in a panel discussion of diseases among the aged, presided over by David B. Allman. The participants, Leland S. McKittrick, Edward C. Reifenstein, Irving S. Wright, and Walter E. Vest Jr., emphasized that, due to changes in physiological functions of the body as a result of the aging process, disease may be masked or produce bizarre and misleading symptoms. An added problem is the frequent tendency of such patients to minimize or neglect complaints that would bring the younger patient to a physician promptly. Special care is required in taking and interpreting the history, as well as in the physical examination. What might be dismissed as minor changes in body function can be of great significance.

Speaking specifically on the problem of cancer in the aged McKittrick emphasized that no patient is too old to be denied treatment, the only real risk to be considered being that of anesthesia. Reifenstein, discussing the general subject of bone disorders, specifically senile osteoporosis, reminded his hearers that this can begin at the relatively early age of 45 years. He pointed out that it may be a preventable disorder, citing the new hypothesis regarding treatment based on findings that anti-anabolic hormone production actually decreased only slightly with advancing age. The possibility of administering anti-ACTH treatment was suggested as one approach.

Wright, discussing atherosclerosis, which he identified as a disease in itself and not an etiology, cited the possible promise in MER-29, shown in experimental studies to hinder cholesterol formation. He emphasized that heredity is always an important factor in the development of atherosclerosis, and that emotional stress may occasionally play a contributing part. Exercise in moderation is good for such patients. It has been shown that the blood cholesterol level actually can be lowered by this type of activity when it is carried out as a continuing daily program. The usefulness of anticoagulants still awaits final evaluation. One problem is the possibility that hereditary factors may be involved in variations of the clotting mechanism from normal.

At later panel discussions of promotion of physical fitness and motivation of the aging E. W. Busse made the important point that members of all health professions, especially physicians, are sorely in need of motivation to understand and help these patients.

A symposium dealing with esophageal hiatal hernia brought together the sections on Diseases of the Chest, Gastroenterology and Proctology, and Radiology. All aspects of this problem, which so far as the general physician is concerned requires a generally higher index of suspicion than is presently apparent, were covered competently from the viewpoint of the internist, the radiologist, and the surgeon. Arthur M. Olsen presented a paper on the role of motility patterns in the diagnosis of esophageal disease. Radiologic aspects were described by Frederic E. Templeton, and endoscopic aspects by Paul H. Holinger.

In considering clinical features of the management of hiatal hernia Charles A. Flood divided patients with this disease into three main groups: those with distress only, those with hemorrhage, and those with obstructive symptoms. Emphasis was placed on conservative management as the desideratum. The symptom of esophagitis, common to all groups, usually presents no serious treatment difficulties. In discussing the surgical considerations in the treatment of hiatal hernia Brian B. Blades said that symptoms are usually progressively severe. Need for surgical intervention has increased partly because of the greater number of older people in our population. Risk of operation is not serious provided proper preoperative and postoperative management is insured.

At a General Practice symposium on viruses, Alexander D. Langmuir described the present status of poliomyelitis vaccine and application of control measures. Data on the role of adenoviruses were provided by Harold S. Ginsberg. Robert Huebner and Leon Rosen presented a discussion of enteroviruses, a group of 51 organisms that apparently are closely related but show wide variations insofar as production of clinical manifestations in patients is concerned. The para-influenza viruses, isolated recently from patients with respiratory illnesses, represent a new group of agents that apparently can be grown satisfactorily only on tissue culture, according to Robert M. Chanock.

All aspects of the problem of gastric ulcer were considered in a symposium participated in by the sections on Gastroenterology and Proctology, Pathology and Physiology, and Radiology. Presentations on the contributions of the physiologist, the pathologist, the radiologist, the clinician, and the surgeon were followed by a general panel discussion.

Sports Injuries

Far more injuries are encountered in physical education classes than in supervised athletic contests, according to Don H. O'Donoghue, coach of the Oklahoma "Sooners" football team, who addressed a symposium on this subject. He emphasized the trend toward greater participation and therefore the need for greater attention to this general subject. The most important single factor in the care of injured players is early detection and accurate identification of the extent of injury.

Allan J. Ryan, Chairman, A. M. A. Committee on Injuries in Sports, revealed that this has now become a year-round activity. One anticipated development is the setting of test standards for various types of helmets used in sport activities. Research centers are being contacted, and surveys are being made of injuries and their management, as well as of training programs for athletes. Available from A. M. A. headquarters for distribution to team physicians and others working in this area are three publications, Protecting the Health of the High School Athlete, A Bill of Rights for the College Athlete, and Safeguarding the Health of the High School Athlete. It was stated that a change in name of the Ryan organization to the Committee on Medical Aspects of Athletics has been recommended as being more indicative of its scope.

According to Andrew Tomb, far too often Little League players have poor medical supervision and protection against injury. Poorly fitting equipment often presents problems. Kenneth B. Rawlinson outlined the duties of a trainer as including prevention, treatment, and rehabilitation. The first properly receives the most attention, and consists of preseason examination, care on the practice field, conditioning (both physical and mental), and good equipment. A basic recommendation made by him was that ankle wrapping be practiced routinely in all forms of contact sports. There is a high incidence of "bad" knees, many of which can be restored to normal function by operation.

Virtually all athletic injuries are the result not so much of direct trauma as of incoordination, according to Robert G. Brashear, who stated his belief that medical consultations on the field of play are unsatisfactory and that team physicians should always have facilities for examination of injured players in privacy.

Medical Color Television

Celebrating its 10th anniversary, closed-circuit color television rose to new heights of interest and perfection, presenting clinical topics to physicians attending the sessions. I. S. Ravdin demonstrated a gallbladder operation and V. Earl Johnson an operation on a thyroglossal duct, in the Monday morning program. A dermatology panel presentation Monday afternoon was presided over by Donald Pillsbury. John R. Heller headed a panel discussion of the cause and treatment of malignant disease on Tuesday morning, and in the afternoon a panel discussion of the possible etiological relationship of viruses to cancer was moderated by Ravdin. The Wednesday morning period was devoted to problems in obstetrics and gynecology, and in the afternoon cardiovascular disease was considered. The panel discussion of the staphylococcic problem described earlier appeared Thursday morning, and in the afternoon Howard A. Rusk was moderator of a panel discussion of the general subject of physical rehabilitation.

Committee on Cosmetics

The Committee on Cosmetics, A. M. A. Council on Drugs, sponsored a symposium on current approaches to the correction of cutaneous disfigurements. The purpose of the symposium was to review the most widely accepted methods for restoration of normal appearance in such disfiguring conditions as acne and hirsutism, as well as various common pigmentary and integumentary disturbances. Carl T. Nelson, chairman, introduced the symposium with a review of the peculiar significance in modern society of aberrations from the normal in appearance. He stressed that strong pressures operate in the environment not only on the disfigured person to seek medical help but also on the physician to provide the best available means of correction. He believes society no longer attributes efforts by disfigured persons to improve their appearance to vanity or self-indulgence. On the contrary, such persons are expected to seek help as a means of minimizing the psychological, sociological, and economic implications of a cutaneous deformity. The physician's responsibility is to provide medical care based on an understanding of the unique problems of a less than normal appearance.

Howard Behrman summarized present concepts of the diagnosis and management of hirsutism. Causative mechanisms of the various forms of hirsutism were described, as well as certain theoretical and practical suggestions recently advanced for control of the condition. In so-called idiopathic hirsutism small amounts of the steroid hormones have recently proved an effective remedial measure subsequent to thorough diagnostic and endocrinologic case study. Dr. Behrman also discussed various measures available at present for the external control of hirsutism, such as the use of depilatories, waxes, and bleaches, as well as physical techniques such as electrolysis and the more currently popular diathermy.

Herbert Rattner and M. Paul Lazar presented a realistic appraisal of dermabrasion based on six years' experience. They summarized such merits of the procedure as simplicity of technique, relative freedom from hazards, absence of mortality, low morbidity, and, in well-selected patients, satisfactory results. A major limitation is that not all types of scars, including many of the most frequently seen, can be improved. Unfortunately the patient with a leathery, pitted, open-pore type of skin, most anxious for and most in need of help, gets practically none from dermabrasion. One of the most important aspects in dermabrasion is the careful selection of patients, based primarily on a critical assessment of the shape, depth, and location of scars. The attitude of the patient toward his disfigurement and what he expects from dermabrasion must also be evaluated carefully.

Otto Stegmaier, discussing the cosmetic management of nevi and pigmentary disturbances, urged that all melanocytic nevi (common moles) be subjected to examination on removal. He also reported on the use of psoralens and monobenzyl ether of hydroquinone, together with nonspecific measures such as sun-screen protective ointments and cosmetic masking creams, in vitiligo and chloasma.

Daniel Kindel reviewed the incidence, time of appearance, rate of growth, clinical appraisal and course throughout life of common types of hemangiomas. He commented particularly on the cosmetic results to be expected in the use of newer forms of low-voltage x-ray therapy (level therapy) for hemangiomas of various sizes and depths. He pointed out the dangers in the current trend to "watch" hemangiomas for spontaneous involution. George Crikelair discussed the problems of the surgeon in the correction of cutaneous disfigurements. He stressed that misconceptions about plastic surgery must not be overlooked. Frequently the idea that plastic surgery is surgery without scar formation must be clarified before treatment. Basic principles involved in electively making facial incisions so as to minimize scar formation were described. The most important stage in therapy directed toward satisfactory cosmetic results is frequently the passage of time. Early surgical correction is advisable for scar contractures, anatomically malaligned structures, and tissue deficiencies.

Council on Foods and Nutrition

The Council on Foods and Nutrition and the Nutrition Foundation, Inc., had a question-and-answer symposium as a part of the scientific exhibit. "Diet as a Preventive and Therapeutic Tool for the Doctor" was the subject of the week-long program devoted to many disease conditions in which diet is of specific importance. Perhaps of greatest popularity were the sessions dealing with diet in relation to coronary vascular disease. It was generally agreed that more attention should be directed toward the content of triglycerides in the serum, especially when a physician attempts to treat a patient with a low-fat high-carbohydrate diet. Triglycerides are increased with this type of dietary regimen. Both triglycerides and b-lipoproteins should be measured, as cholesterol levels may not always give a reliable indication of the lipid content of the blood. Simple reduction of fat intake has not been found to be an effective means of lowering serum cholesterol levels. To be effective, 40% of the total caloric intake should be supplied by fat and 75% of this by unsaturated fat. Inexpensive vegetable oils are good sources of unsaturated fatty acids.

At a session on management of diabetes mellitus the use of sorbitol in the diet was discussed. Sorbitol does not increase glucose levels in the blood, because of its slow absorption and the release of fructose in the liver. Therefore, use of sorbitol is of value in the diet of the young diabetic to help avoid overnight hypoglycemia.

Carl V. Moore pointed out that diet is of greater importance in preventing most anemias than in their treatment. Megaloblastic anemia, a folic acid deficiency, is most often found in patients who are food faddists, in women with pernicious anemia of pregnancy, in pregnant patients who do not ingest a good diet, in patients with steatorrhea, and in some formula-fed infants. True pernicious anemia only rarely develops as a result of diet.

Much interest was shown in the seven sessions on weight control. Hilde Bruch of Columbia University, in discussing the motivation of the patient to reduce weight, said that special diets give significance and dignity to weight-reduction programs. Albert Stunkard of the University of Pennsylvania maintained that treatment for obesity is remarkably ineffective. Although fine methods for weight reduction are available, patients just do not follow them.

Diet in the management of injury was discussed by Stanley Levenson of Walter Reed Army Institute of Research. Response to injury is conditioned by the nutritional reserve of the patient. Levenson reported that patients with severe injuries show great and continuous nitrogen loss on low-protein diets. Calcium loss after severe injury is about the same as that from bed rest per se; however, this loss does not appear to interfere with bone healing in the case of patients with fractures. General recommendations on diet in treatment of severe injury in a young adult male are 60 calories, 2 to 4 Gm. of protein, and 1 to 2 Gm. of vitamin C per kilogram of body weight. Dr. Levenson recommended that 40 to 50% of the total calories be supplied by fat.

Donald Watkin, of the National Institutes of Health, noted that an aged person may have different protein requirements, because of either a greater need for essential amino acids or a lessened ability to synthesize the nonessential amino acids.

It is important to know the minimum requirement for protein, since renal excretion of nitrogen may be more difficult in the aged. This is of particular importance when proteins of low biological value are consumed.

Highlights of the scientific sessions were telecast each evening Monday through Thursday from the convention hall through the cooperation of Merck Sharp & Dohme. The 30-minute A. M. A. Bulletins of the Air were broadcast live in Philadelphia and Atlantic City. Two of the programs were telecast in New York, Boston, and Washington.

Scientific Exhibits

Many of the scientific exhibits have been discussed in connection with various symposiums and special lectures. So far as interest and value is concerned, all deserve mention for their significant contribution to a week of concentrated "brush-up" that all physician visitors found highly satisfying.

A presentation of geriatrics for the generalist, dealing specifically with management of the difficult geriatric patient, had a pertinent application in that care of the aged may become a major part of medical practice.

Striking reminders for all physicians were contained in an exhibit emphasizing that they have an important role in the prevention of home accidents. Useful suggestions on how to initiate a communitywide program were provided in graphic form.

Thought-provoking reminders were contained in an exhibit on the uses and abuses of blood transfusion. It was shown that this procedure is still accompanied by considerable potential risk, that errors still occur in selection of blood for transfusion, and that there is still a chance of transmitting disease in this way. Another exhibit detailed acceptable blood transfusion standards, and still another dealt with the prevention of transfusion reactions through the new approach of combining a soluble form of prednisolone with the transfused blood.

An interesting new approach to the treatment of emphysema was described in an exhibit containing details of a tracheal fenestration operation. Reminders of the growing problem of air pollution were contained in a map exhibit showing air sampling sites in the United States. Air sampling filters also were shown. Among the adverse effects listed were nuisance, soiling, irritation, corrosion, reduced visibility, and damage to plants and animals.

Transfusion treatment of cancer by isolation of the involved limb and perfusion of it with nitrogen mustard was described in a graphic exhibit.

Motion Picture Program

The Monday-through-Friday film program presentation, arranged by Ralph P. Creer, manager of the Department of Medical Motion Pictures and Television, was up to its usual standard of excellence. In addition to films already discussed in connection with special events, it may be mentioned that the film on causes of abdominal pain, prepared by Hilger P. Jenkins and discussed by a panel of which Warren H. Cole was moderator, drew a capacity audience. A film on cardiac arrest, prepared by J. Beard of London, had its premiere American showing before a large audience. Especially good photography characterized a film on culdoscopic technique and cinematography. Much interest was shown by visiting physicians in a film showing details of a complete office gynecologic examination, as well as a companion film on routine pelvic examination and methods of cytological study. A film prepared jointly by the A. M. A. and the American Bar Association on in-hospital professional liability action provided much useful guidance. All specialties were represented in the 53 films presented during the five-day period.

Award Winners

Hektoen Medals.—Hektoen medals, presented for exhibits of original investigation and judged on the basis of originality and excellence of presentation, were awarded as follows:

Gold medal—Oscar Creech Jr., E. T. Krementz, R. F. Ryan, Keith Reemtsma, J. N. Winblad, and James L. Elliott of Tulane University School of Medicine, Charity Hospital, Touro Infirmary, and the U. S. Public Health hospital, New Orleans, for the exhibit on treatment of cancer by perfusion.

Silver medal—James L. Tullis, L. L. Haynes, Hugh Pyle, Stanley Wallach, Robert Pennell, Mary T. Sproul, and A. Khoubesserian, Protein Foundation and U. S. Naval Hospital, Boston, for the exhibit on clinical use of frozen red blood cells.

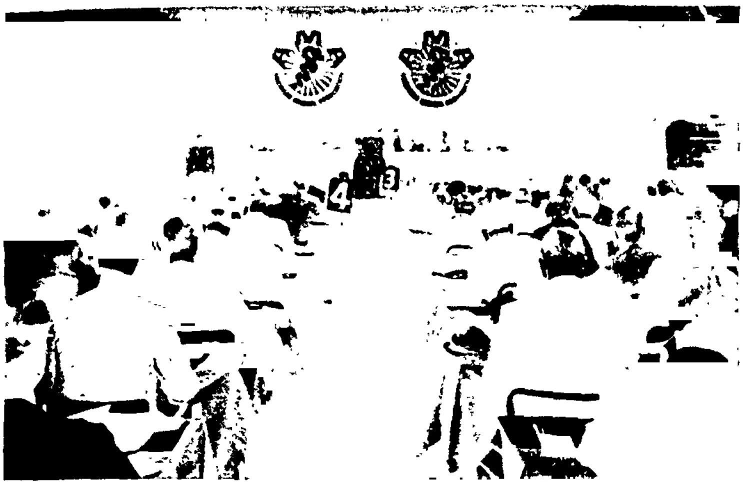
Bronze medal—Arild E. Hansen, Hilda F. Wiese, Arr Nell Boelsche, Mary Ellen Haggard, Doris J. D. Adam, and Helen Davis, University of Texas School of Medicine, Galveston, for the exhibit on linoleic acid in infant feeding and the significance of linoleic acid in the diet of infants.

Billings Medals.—Gold medal to J. Brown Farrior and Robert L. Levine of Tampa, Fla., for the exhibit on ear surgery in 3D; tympanoplasty, stapes, and fenestration.

Silver medal to Arnold P. Friedman, Charles A. Carton, and Asao Hirano of Montefiore Hospital, Bronx, N. Y., for the exhibit on facial pain.

Bronze medal to Philip Schwartz, Warren State Hospital, Warren, Pa., for the exhibit on cerebral apoplexy, its types, causes, and pathogenesis.

Scenes from the Atlantic City Meeting



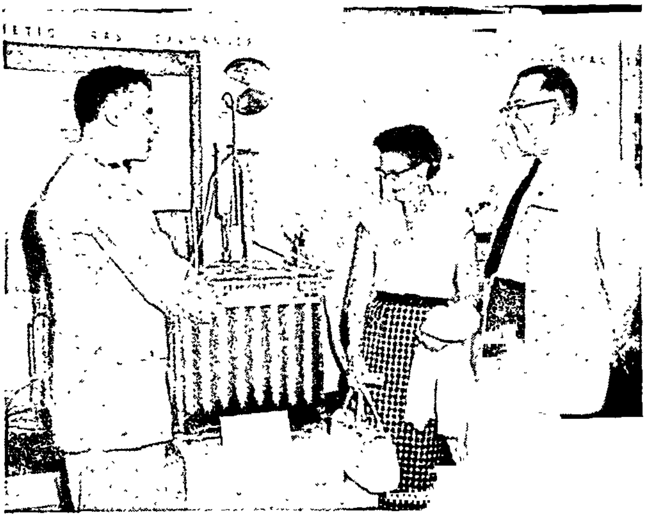
Left, House of Delegates in session during American Medical Association's 108th Annual Meeting in Atlantic City, June 8-12, 1959.

In photo at right Dr. John S. De Tar (*center*) stands, during all-day session of special reference committee which he headed, to report on long-awaited findings of Commission on Medical Care Plans.

Dr. M. Louise C. Gloeckner of Conshohocken, Pa. (*arrow*), only woman delegate of A. M. A. House, is surrounded by male colleagues during deliberations on Social Security coverage.

Dwight D. Eisenhower, first United States President to address an A. M. A. Convention, is greeted at airport by (*left to right*) Drs. Leonard W. Larson, re-elected Chairman of Board of Trustees, Louis M. Orr, new A. M. A. President, and Gunnar Gundersen, retiring A. M. A. President.

Science and Exhibit . . . .

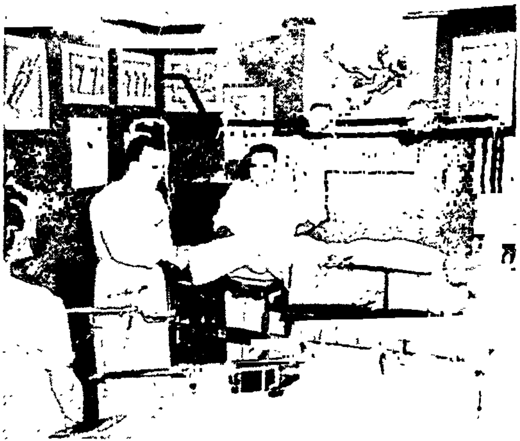


Operation of photosynthetic gas exchanger was feature of exhibit on Space Medicine Research. Capt. Jack Bates of space medicine division, Randolph Air Force Base, Texas, points out its uses to Dr. and Mrs. George Hamerick Jr. of Fort Lauderdale, Fla.

Dr. Dan M. Gordon's exhibit, "The Inflamed Eye," composed of large-scale eye model and coordinated transparencies, is explained to Dr. D. D. Sandersen (*right*) of Lincoln, Neb.

Huge plastic reproduction of human cell draws attention of Dr. and Mrs. H. C. Halsted of Plainfield, N. J. Exhibitor explains its construction and features.

Dr. Robert Breckenridge of Glenside, Pa., points out diseased areas of fresh pathological specimens to Dr. Carl V. Anderson of Warwick, R. I.



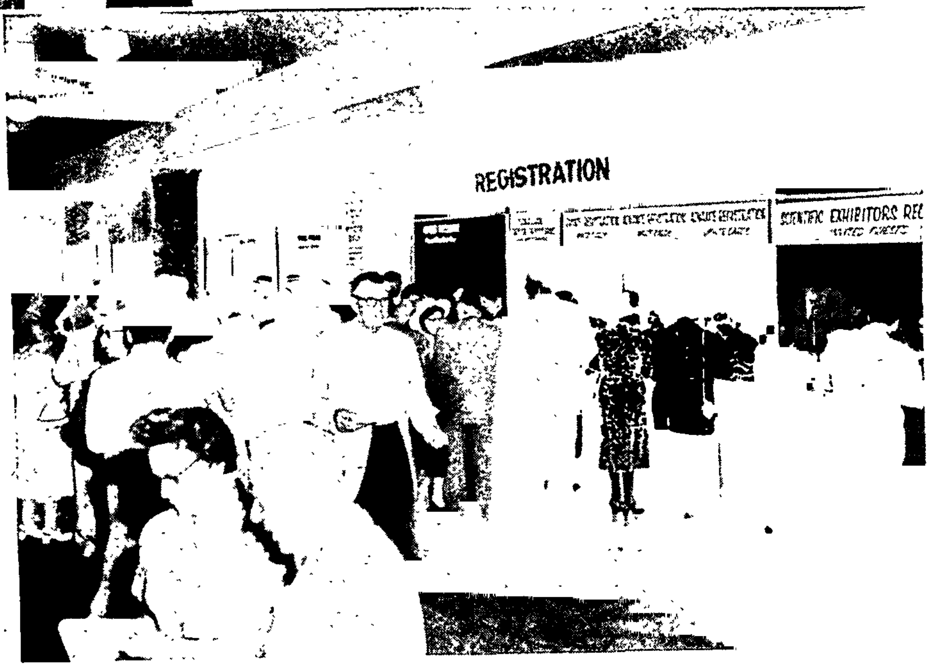
Drs. Sydney N. Lyttle of Flint, Mich., and Paul S. Miller with medical student (*lying down*) in scientific exhibit.

Awards and Honors . . . .

At left, Dr. Carl V. Moore (*center*), winner of Goldberger award in clinical nutrition, receives congratulations of retiring A. M. A. President Gunnar Gundersen (*left*) and Dr. Walter L. Bierring (*right*), at presentation in Traymore Hotel.

Shown above, Francis Boyer (*left*), chairman of board of Smith Kline & French Laboratories, accepts award for pioneering in medical color television from Dr. Leonard W. Larson.

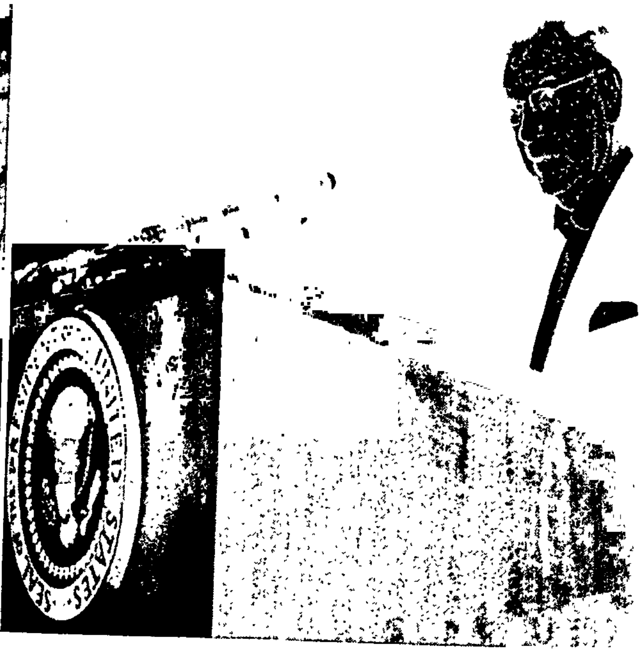
Dr. Louis M. Orr (*left*), new A. M. A. President, displays Distinguished Service award given to Dr. Michael De Bakey (*right*) of Houston.



The 108th Annual Meeting began when thousands of physicians registered at Convention Hall, where almost 700 exhibits were displayed.

Sessions—Formal and Informal . . . .

Dr. Howard M. Snyder, President Eisenhower's personal physician, receives applause of 5,000 guests at Inaugural Ceremony.



Dr. E. Vincent Askey, as Speaker of House of Delegates, addresses Inaugural Ceremony audience. He was later named President-elect.

Left, President Eisenhower chats with science fair winners Edith K. Schuele of Memphis, Tenn., and Martin Murphy of Canon City, Colo. They were brought to Atlantic City meeting under A. M. A. auspices.

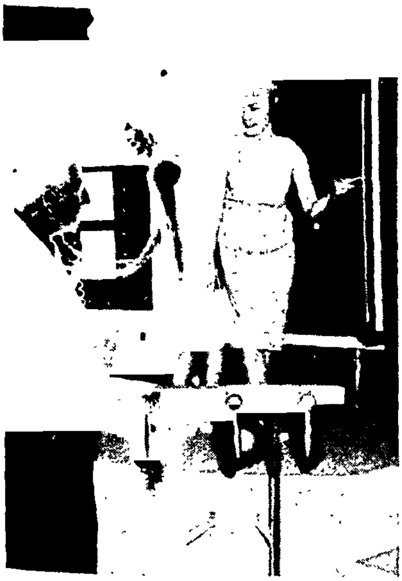
Right, three members of five-man Judicial Council discuss osteopathy question in preconvention session.

Diversion Amid Study . . . .

At right, Martha Wessner (*left*) and Sandra Egli of Evansville, Ind., representing Vanderburgh County (Ind.) Medical Society and Evansville Museum of Arts and Sciences, demonstrate antiquated drug mill in exhibit showing medical practice 100 years ago.

In photo at left, Drs. Frank O. Hendrickson, Springfield, Pa., past-president of American Medical Golfing Association (*left*), and James McLaughlin, Philadelphia, president, examine golf scores.

Left to right, Drs. R. W. Lamong-Havers of New York, Fred J. Fagan of New London, Conn., and John W. Sigler of Detroit review literature in joint exhibit symposium of American Rheumatism Association and Arthritis and Rheumatism Foundation.



Dr. Bernard Sherman of Cedar Grove, N. J., listens over telephone to story of new antidepressant agent as Susan Gilbert (*left*) and Donna Rhodes of Philadelphia tell it in pantomime.

Right, Dr. and Mrs. Frank Sirulnik of Springfield, Mass., admire Dr. Eric P. Mosse's sculpture, "Happy Girl," cited best of show at American Physicians Art Association annual exhibit.

COUNCIL ON MEDICAL SERVICE

METHODS FOR THE PRESERVATION OF PRIVATE MEDICAL PRACTICE

Claud J. N. Weber, Boston

The United States has achieved a position of greatness by developing its resources under a private enterprise system. The discoveries, inventions, and developments engendered by competition among individuals, partnerships, corporations, and associations has brought about tremendous advances in all lines of endeavor so that today we stand at the pinnacle of all nations of the world.

There is a vital place in this system for government, the duty of which should be to regulate, guard against, and punish wrongdoing, but never to substitute government ownership and operation in the place of private ownership and operation and thus destroy the competitive private enterprise system. That is my personal philosophy.

The topic for discussion is methods for the preservation of private medical practice. The term "private medical practice" is not easy to define. An over-simplified definition might be "complete freedom of choice by both doctor and patient." But, in any God-fearing nation there is no such thing as complete freedom of choice without any restraints. We are restrained by the commandments of God, the dictates of conscience, the laws of the community, and the rules of society. However, subject to proper regulations for admission to practice and to the normal rules of the medical society, a doctor should be free to enter practice wherever he may choose, to practice whatever hours he selects, to specialize in whatever field he desires, and to charge whatever he believes is proper. A patient should be free to seek out any doctor he chooses for his medical needs and to agree on any fee he thinks is fair. That is my idea of the private practice of medicine; anything that tends to destroy that freedom of choice tends also to destroy the private practice of medicine.

Perhaps we should ask: "Should the private practice of medicine be preserved?" I'm sure you know my answer, but for the purpose of discussion there are three preliminary questions that must be resolved to find the answer to the main question. These are the following: 1. What is best for the general public? 2. What is best for the medical profession? 3. What is best for the advancement of medical science?

The medical profession in this country has engaged in extensive research for many years to find the correct solution to the problem of providing adequate medical care under a system that would be within the reach of all. Everyone should keep in mind that, if necessary, medical care can be provided adequately under a free enterprise system; there is no need for socialized medicine and the proponents are without logic to support their plan.

From the beginning study of the American Medical Association years ago, there finally arose convictions that there were private means, as distinguished from public funds, which could to a large degree be used to provide medical care for people of modest means. The four recognized major categories for providing the means for this medical care were individual insurance underwriters, group insurance underwriters, Blue Cross and Blue Shield plans, and the so-called independent plans.

Values for the General Public

I sincerely believe that the best interest of the general public requires the continuation of our system of the private practice of medicine and steadfast opposition to a system of socialized medicine. The thought exists in the minds of many that socialized medicine brings about the means for complete medical attention without any cost to them. That is ridiculous. Under socialized medicine the general public must pay the bill. The government can get the funds only by taxation of the people. The people must pay for socialized schemes and often very dearly and at a loss to personal initiative, personal choice, personal responsibility, and the high efficiency that a free operating competitive system brings.

The need for medical attention by segments of our population and the necessity for financial aid to meet the costs of such medical care has been recognized by the American Medical Association as one of the arguments of the proponents of nationalized medicine. Funds which are provided by any private source, whether by insurance contract, Blue Shield, or some independent plan to defray the

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Third vice-president, Lumbermens Mutual Casualty Company, and claims manager, New England department of the Kemper Insurance companies.

Read before a meeting of the Norfolk Medical Society, Dorchester, Mass., Jan. 27, 1959.

cost of necessary medical attention (unless they prohibit freedom of choice), are actually funds which are helping to protect our national system of the private practice of medicine.

It is the purpose of sound health insurance programs to meet public demands and public needs and yet preserve complete freedom of physician selection on the part of the patient. The insurance industry is cognizant of the fact that the physician-patient relationship, based on freedom of choice, is essential to all that is good in the private practice of medicine.

Do I mean that insurance policies and other programs providing for medical reimbursement are not a desirable development? Certainly not, for they are outstanding developments for the public good under our democratic system of private enterprise. I mention this because I do not believe it is necessary or advisable to provide complete medical care, without any cost to the individual, such as is claimed for socialized medicine, any more than it is necessary or advisable for the government to take over the grocery business to make sure that everyone has enough to eat or the type and quantity of food a bureaucrat thinks would be best for them. In a democracy something must be left to the personal initiative and the personal choice of the individual, and the best results will generally follow where the individual has some personal financial interest in the changes and some direct personal financial interest in the outcome.

At the same time, we should make every effort to put within the reach of the majority of our people a program whereby they may protect themselves against substantial financial loss due to accident or illness. In a free society a man should be permitted to decide what part of the risk he wishes to assume personally.

Let us see what has been accomplished with this basic ideal of making adequate medical care available to all within reasonable limits consistent with our tradition, our standards of living and our way of life. Tremendous progress has taken place under our free-enterprise system. The Health Insurance Council report of Dec. 31, 1956, states that the number of persons with hospital expense insurance increased from 12,300,000 in 1940 to 115,900,000 in 1956, the number with surgical expense protection rose from 5,300,000 to 101,300,000, and the number with medical expense protection rose from 3,000,000 to 64,900,000.

The 12th annual survey of the Health Insurance Council, Dec. 31, 1957, indicates that the number of persons covered for hospital expense increased 4.7% over that of 1956, to 121,432,000; the number covered for surgical expense rose 7.5%, to 108,931,000; and the number protected against regular medical expense increased 10.7%, to 71,813,000 persons. The number of persons covered is increasing by the millions each year; this I think largely tells the story of the success of our free enterprise system in dealing with the medical needs of our people.

Competition in the field of health insurance is extremely keen. Each company tries to make its policies the best. Each company tries to offer the broadest coverage, to provide the most attractive limits, to give the best service, and to have the most satisfactory premium charge. This competition has produced and will continue to produce wonderful advancements in the field of health insurance—all to the benefit of the general public.

Reviewing this record, can any fair minded person give any other answer than that the competitive system of private enterprise is by far the best for the welfare of the American people? One should never forget that competition in private enterprise is the life blood of a democracy and through this competition wonderful advancements and developments have taken place both in relation to products and services.

Values for the Medical Profession

My second question was, "What is best for the medical profession?" What has been said in answer to the first question applies to the medical profession as well. A doctor friend of mine, who recently returned from England, wrote me as follows:

> I have two physicians here at the hospital who formerly were physicians in England and a friend of mine recently returned after a year's leave working in a hospital in Scotland. The three of them have bitter personal feelings about the operation of the health plan in England. They all say it decreases initiative on the part of the doctor and that it is enormously expensive to administer, both from the point of view of what the individual citizen has to contribute each week and the high cost of the government administration of it.

Since any one of you can perhaps better answer the question as to what socialized medicine might do to your individual initiative as a doctor and to your practice of medicine, I will leave the second question here with the observation that socialized medicine would probably destroy much that is good, desirable, and wholesome in the medical profession today and would probably leave it bitter and embroiled in the machinations of politics.

Advancement of Medical Science

The third question I raised was, "What is best for the advancement of medical science?" Through the years medical science has made wonderful advancements in America. There is nothing to indicate that it would have done better under a system of socialized medicine. There is much to indicate that it could not have done as well.

The American people and American business have responded generously for the advancement of medical science through the years; witness the response of the public to the special drives for funds to combat poliomyelitis, heart disease, tuberculosis, multiple sclerosis, and other diseases. An article in the February, 1959, issue of *Reader's Digest* indicates that donations to the Heart Association have risen from $100,000 in 1941 to 20 million dollars, and the Cancer Society collected 30 million dollars in 1957 compared with $800,000 in 1944. Witness the financial contributions of business and industry for medical research and medical education by such organizations as the Carnegie Corporation, the Commonwealth Fund, the Hood Foundation, the Kemper Foundation, the Macey Foundation, the Rockefeller Foundation, the Whitney Foundation, the American Medical Educational Fund, the Medical Education Foundation, the National Fund for Medical Education, the Ella Sach's Plotz Foundation, the Post Graduate Medical Institute, and the Sears Roebuck Foundation. There is no need for socialized medicine for the advancement of medical science in America. Contributions by individuals, business, and industry and government grants without strings attached will take care of the financial needs in a manner which is in keeping with our American way of life.

Despite the fact that every impartial analysis indicates that the best interests of the general public, the best interests of the medical profession, and the advancement of medical science requires the continuation of the principle of the private practice of medicine, constant vigilance is necessary. It means that the medical profession, other professions, business, industry, and labor must unite in an effort to preserve the private practice of medicine. The insurance industry and its representatives are not without their faults, but by working closely together, in a spirit dedicated to the preservation of our system of private enterprise, we should be able to solve all major problems for the best interests of all and in keeping with our American way of life.

Preservation of Private Medical Practice

At last I come to the methods for the preservation of private medical practice.

Your medical societies across the land have debated this question and have come up with many excellent suggestions. These deal primarily with the doctor-patient relationship, medical facilities, treatments, charges, the elimination of any abuses, and the disciplining of the small number of physicians who fail to live up to the high standards of the medical profession.

There is one other method for preserving the private practice of medicine that seems to have been generally overlooked. I believe it to be vitally important and I will bring it to the front by asking a question. For many years, bills have been pre- some phase of the insurance business. Their pur- sented to our legislature to create a state fund for pose was to have the state government take over some part of the insurance business, and this would clearly be an entering wedge for the socialization of the insurance industry.

Is there a single doctor in this room who raised his voice in opposition? Is there one doctor who called his state representative or state senator and asked him to oppose such legislation? Democratic processes have been destroyed before while responsible citizens slept. It is but one step from socialized insurance to socialized medicine. You should not strive to protect the one and ignore all others.

I propose that you individually take a direct interest in good government, that as individuals and as a group you make your voices heard, that you set up within your association some watchdog procedure so that you may know what is being proposed in our legislature and then, both as individual citizens and as an important association, become articulate in defense of what you believe to be right. Openly, diligently, and whole-heartedly support those candidates who stand for the things you believe in, not only as they relate to the practice of medicine but also as to other normal activities; ask your patients, your neighbors, and your friends and acquaintances to do likewise. Demand to know where candidates stand on vital issues, and oppose with all your vigor those who advocate the destruction of the free enterprise system. Socialism is like a dreaded disease—once it invades a vital organ you may not be able to cut it out without destroying the patient.

Through the ages the power and influence of the doctor have been enormous. Individuals and families look up to their doctor with respect and confidence. As they trust to your judgment with their lives, they will trust your judgment in other things. The doctor of medicine holds an exalted place in the minds and hearts of a nation. Not only in the practice of medicine but in other things, the doctor stands in an excellent position to contribute greatly to the welfare of mankind.

There is only one place where your right to engage in the private practice of medicine can be taken away from you and that is in our legislature or in a referendum by all the people. You have the power to yield tremendous influence for good if you will but awaken and make your voices heard.

MEDICAL NEWS

ALABAMA

Dr. Sussex Appointed Psychiatry Chairman.—Dr. James N. Sussex, formerly associate professor of psychiatry at the University of Alabama Medical Center, Birmingham, has been named professor and chairman of the department of psychiatry. Dr. Sussex, whose appointment became effective May 1, replaces Dr. Elmer L. Caveny, who has resigned as chairman of the department to enter private practice. Dr. Caveny will remain as a professor of psychiatry on a part-time basis. Dr. Sussex joined the staff of the Medical Center in 1955. Prior to this time, he was assistant in clinical psychiatry at Georgetown University School of Medicine in Washington, D. C. He is a diplomate in psychiatry of the American Board of Psychiatry and Neurology.

CALIFORNIA

Dr. Carpenter to Lecture in Spain.—Dr. Charles M. Carpenter, professor of infectious diseases and chairman of the department, School of Medicine, University of California, Los Angeles, has been awarded a fellowship from the Del Amo Foundation for six weeks of lecturing and carrying out studies on brucellosis in Spain. Last year Dr. Carpenter was similarly honored by the foundation. Dr. Carpenter's work will be carried out in Madrid and in Northern Spain, Pamplona, Province of Navarra. He will also participate in the 16th International Veterinary Congress, to be held in Madrid. The Del Amo Foundation, founded by Dr. Del Amo, is endowed to improve the scientific and cultural relationships between Spain and Southern California, for which the foundation sponsors an exchange fellowship program.

CONNECTICUT

Formal Incorporation of Medical Center.—The Yale School of Medicine and the Grace-New Haven Community Hospital, affiliated with each other since 1826, announced the formal incorporation of the Yale-New Haven Medical Center aimed at a major expansion of the patient-care facilities of its university hospital services. Elected first president of the new Medical Center Corporation is Mr. Charles S. Gage, treasurer of Yale University. Others named to the Governing Board are Mr. George S. Stevenson, president, Grace-New Haven Community Hospital; Mr. Paul M. Zorn, vice-president, Southern New England Telephone Company; Dr. Albert W. Snoke, director, Grace-New Haven Community Hospital; Dr. Vernon W. Lippard, dean, Yale School of Medicine; and Mr. Charles M. O'Hearn, assistant to the president of Yale. The 133-year old partnership between Yale and the hospital was first expanded into an informal Yale-New Haven Medical Center operation in 1954. A chief objective of the incorporation is to broaden the efforts of the Medical Center in acquainting more community physicians and patients with advanced medical and surgical treatments, according to Mr. Gage. The formal incorporation will aid the Medical Center in seeking support for extensive research work being conducted to develop new methods of treatment for patients.

MINNESOTA

Dr. Bickford Wins Travel Award.—Dr. Reginald G. Bickford, head of the electroencephalographic laboratories, Mayo Clinic, Rochester, was the recipient of a travel award, conferred by the Institute of Radio Engineers, for his paper, "An Automatic System for the Recognition of a Spike-and-Wave Discharge," which he presented at the International Congress on Medical Electronics in Paris, France. Dr. Bickford attended the annual meeting of the American Electroencephalographic Society at Atlantic City, N. J., and a conference on "Data Processing in Medical Research" at Poughkeepsie, N. Y. He also visited London, England, before attending the international congress in Paris. He will return to Rochester on July 4. Dr. Bickford, born in Brewood, England, came to Rochester in 1946 as a research associate in the Mayo Foundation.

MISSISSIPPI

Dr. Hill Becomes President.—Dr. Stanley A. Hill, Corinth, was inaugurated president at the 91st annual session of the Mississippi State Medical Association after delegates named Dr. Gilliam S. Hicks, Natchez, *president-elect*. Dr. Hill is the first president in MSMA's 103-year history to follow his father in office, Dr. J. R. Hill having served in 1935.

NEW YORK

Dr. Johnson Gives Lecture.—Dr. Victor Johnson, director of the Mayo Foundation for Medical Education and Research, Rochester, Minn., delivered the Weiskotten Lecture at the 84th annual Alumni Day held June 6, at the State University Upstate Medical Center, Syracuse. Dr. Johnson's lecture

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Physicians are invited to send to this department items of news of general interest, for example, those relating to society activities, new hospitals, education, and public health. Programs should be received at least three weeks before the date of meeting.

topic was "Evolution of a Doctor." He has been director of the Mayo Foundation and professor of physiology at the University of Minnesota since 1947.

New York City

Radioactive Isotope Course for Technicians.—The Queens Hospital Center of the Department of Hospitals, City of New York, has announced a Course in Radioactive Isotopes for Technicians. The course will consist of eight sessions of four hours each, to be held every Wednesday afternoon, starting Sept. 30 and ending Nov. 25 (1-5 p. m.). The course will be devoted to laboratory techniques in the use of radioactive isotopes, and sessions will be divided equally between lectures and laboratory work. Medical applications of isotopes and health and safety measures will be stressed. Enrollment is limited to 10 members and the tuition fee is $100. For applications write Dr. Philip Kahan, Supervising Medical Superintendent, Queens Hospital Center, 82-68 164th St., Jamaica 32, N. Y.

Report on Tuberculosis.—The New York Tuberculosis and Health Association, Inc., has reported that New York City, which has almost 5% of this nation's population, last year accounted for 8.7% of the new tuberculosis cases found throughout the continental United States. In addition, this city has 7% of all the deaths attributed to tuberculosis throughout the country. A total of 5,482 persons with previously undetected cases of tuberculosis was reported in New York City last year. Provisional figures for the nation as a whole showed 63,300 new active cases. The 833 persons who died from tuberculosis in this city last year compared with 11,950 for the nation as a whole. As has been true for the past several years, Manhattan in 1958 had the highest number of patients with new tuberculosis cases—2,602—of any of the city's five boroughs. Another 1,501 new cases came from Brooklyn. A total of 751 was reported in the Bronx; Queens showed 559, and Richmond (Staten Island) recorded 69. Both the total number of new cases and of tuberculosis deaths showed a decline in this city last year as compared with 1957 (6,117 new cases and 982 deaths). A total of 18,747 New York City residents received treatment for tuberculosis last year. This figure includes persons whose cases were detected in previous years and who were still under treatment in 1958.

NORTH CAROLINA

Dr. Ruffin Honored.—Dr. Julian M. Ruffin, professor of medicine, Duke University Medical Center, Durham, was honored in Atlantic City, June 5, by past and present postgraduate fellows whom he has trained at Duke since 1943. A dinner in recognition of Dr. Ruffin's contributions to training and research in gastroenterology was given by his former students during the annual meeting of the American Gastroenterology Association. Dr. Ruffin was presented with a scroll and an inscribed silver tray at the dinner. Dr. Ruffin served as president of the American Gastroenterology Association during 1953-1954. He is a member of the editorial board of *Gastroenterology*, an area consultant to the Veterans Administration, and a member of the study section in medicine of the National Institutes of Health. Dr. Ruffin has been associated with the Duke University Medical Center since its opening in 1930.

OHIO

Dr. Bond Elected Dean.—Dr. Douglas D. Bond was elected dean of the School of Medicine at the meeting of the Western Reserve University Board of Trustees June 4. In addition, Dr. Joseph T. Wearn, presently dean of the school, was appointed to the newly-created post of vice-president for medical affairs. Both Dr. Wearn and Dr. Bond will assume their new duties Sept. 1. Dr. Bond came to Western Reserve in 1945 as professor of psychiatry and director of the division in the University Hospitals from Army Air Force Headquarters, Washington, D. C., where he has been chief consultant and director of psychiatry. Dr. Wearn, dean of the university's School of Medicine since 1945, has been professor of medicine since 1927 and was director of the department of medicine at University Hospitals from 1929-1957.

Dr. Maloney Comes to Cleveland.—Dr. Walter H. Maloney holds the appointment of associate professor and director of otolaryngology at Western Reserve University, Cleveland. He is also director of the division of otolaryngology, department of surgery, University Hospitals of Cleveland. Dr. Maloney was formerly head, department of laryngology and bronchoesophagology, Hahnemann Medical College and Hospital, Philadelphia. In addition, he was director of otolaryngology at Lower Bucks County Hospital, Bristol, Pa., and head of the department of bronchoesophagology at Episcopal Hospital, Northeastern Hospital, and Albert Einstein Medical Center, Northern Division, Philadelphia. He will continue as a guest lecturer in the Graduate School of Medicine, University of Pennsylvania.

OREGON

Dr. Dunphy to Lecture in London.—Dr. J. Englebert Dunphy, recently appointed chairman of the surgery department at the University of Oregon Medical School, Portland, will deliver the Lord Moynihan Lecture before the Royal College of Surgeons in London July 8. He is the 11th American doctor to be honored by an invitation to deliver this biannual lecture, established in 1937. One of the Americans previously honored was Dr. Dunphy's immediate predecessor at the Medical School, Dr. William K. Livingston, who spoke before the Royal College in 1947. Dr. Livingston retired as department chairman in 1958. Dr. Dunphy's subject will be "The Nature and Care of Wounds." On June 25, Dr. Dunphy discussed wound healing in a speech at Queens University, Belfast, Northern Ireland, as part of the university's distinguished scholar program.

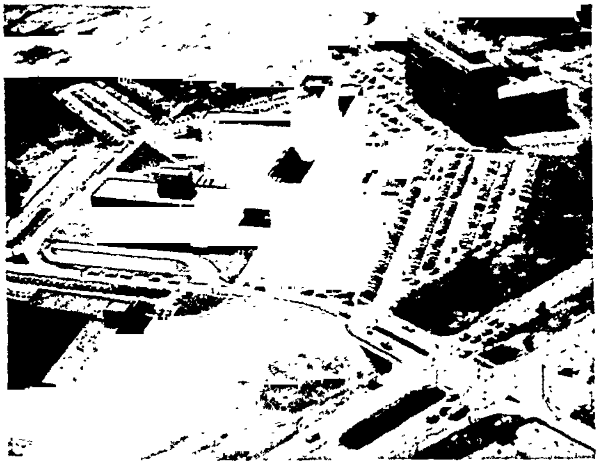
PENNSYLVANIA

Philadelphia

Dinner Honors Dr. Ravdin.—A dinner was held June 8 as a tribute to Dr. I. S. Ravdin, vice-president for medical development and John Rhea Barton Professor of Surgery, University of Pennsylvania, to signify the efforts of a group of his personal friends to raise $1,500,000 toward construction of the $5,900,000 I. S. Ravdin Institute addition to the hospital of the university. The institute goal is part of the $7,472,000 total medical center campaign, currently being conducted by the university, which also includes the new $1,572,000 residence for students of the Hospital School of Nursing. The main speaker for the evening was Dr. Leroy E. Burney, surgeon general, U. S. Public Health Service.

TEXAS

Dedicate Clinical Science Building.—Dedication ceremonies for the Clinical Science Building at the University of Texas Southwestern Medical School, Dallas, were held April 16. The building provides for all the clinical departments of the School of Medicine, offices and laboratories, and space for most of the basic science departments and student health service. The building provides about 117,000 square feet of floor space, and was constructed at a cost of $3,500,000. It is divided into nine floors and is physically attached to the four-floor Basic Science Building which was occupied in 1955. Presiding at the dedication ceremonies was Dr. A. J. Gill, dean, Southwestern Medical School. Logan Wilson, Ph.D., president, University of Texas, was a speaker, and Dr. Melvin A. Casberg, vice-president for medical affairs of the university, gave the dedicatory address.



The new Clinical Science Building (upper right), Southwestern Medical School of the University of Texas, Dallas, with the Parkland Memorial Hospital of the Dallas Hospital District (center) and the staff quarters of Parkland Memorial Hospital (left).

GENERAL

Meeting on Ultrasonics in Medicine.—The American Institute of Ultrasonics in Medicine will hold its annual meeting Sept. 2 at the Leamington Hotel, Minneapolis. The guest speaker at the luncheon meeting will be Dr. H. Russell Meyers, chairman, division of neurosurgery, State University of Iowa Hospitals and College of Medicine, Iowa City, who will present "The Potentials of Ultrasonics in General Surgery and Surgical Specialties." For information, contact Dr. John H. Aldes, Secretary, 4833 Fountain Ave., Los Angeles 29.

Meeting on Facial Plastic Surgery.—The American Society of Facial Plastic Surgery will hold a meeting July 17 at the Hotel Elysee, New York City. The program will include a discussion, "The Role of Psychiatry in Plastic Surgery," and a practical demonstration, "Some Aspects of Hypnosis Applicable to Plastic Surgery," by Dr. Conrad Gale, liaison psychiatrist, The Mount Sinai Hospital, New York City. Dinner ($10) will be served at 7 p. m. For information, write Dr. Samuel M. Bloom, 123 E. 83rd St., New York 28, Secretary.

Open Conference on U. S. Pharmacopeia.—On July 7-8 an open conference will be held on the United States Pharmacopeia XVI. The conference will be concerned with the entire monograph section of the U. S. P. XVI which will be available shortly in page proof. Also considered will be the new or principal chapters of the section on "General Tests." Items will be taken up in sections according to the respective U. S. P. subcommittee assignments. Meetings will be held in the Commodore Hotel and Pharmacopeia Building. For information, write the United States Pharmacopeia, 46 Park Ave., New York 16.

Fellowship for Psychoanalytic Training.—A $5,000 fellowship is available to psychiatrists applying for the full course of psychoanalytic training in the American Institute for Psychoanalysis. The recipient of the fellowship will be granted $2,500 per annum during the second and third years of the training period. In his first year the fellow will attend staff conferences of the Karen Horney Clinic. During the second and third year, he will do five hours of therapy with clinic patients each week and will have one hour of supervision per week. Physicians are eligible to apply who are graduates of an A. M. A. accredited medical school and have completed a one-year general internship and two years psychiatric residency in hospitals approved by the A. M. A. Information, curriculums, and application forms may be obtained from the Registrar, Miss Janet Frey, American Institute for Psychoanalysis, 220 W. 98th St., New York 25.

Prevalence of Poliomyelitis.—According to the National Office of Vital Statistics, the following number of reported cases of poliomyelitis occurred in the United States, its territories and possessions in the weeks ended as indicated:

Area	June 6, 1959		June 7, 1958 Total
	Paralytic Type	Total Cases	
New England States			
Maine	..	..	..
New Hampshire	..	..	..
Vermont	..	..	..
Massachusetts	..	..	..
Rhode Island	..	..	..
Connecticut	..	..	1
Middle Atlantic States			
New York	2	2	3
New Jersey	1	1	..
Pennsylvania	..	..	..
East North Central States			
Ohio	..	2	..
Indiana	..	..	..
Illinois	1	1	1
Michigan	..	2	1
Wisconsin	..	..	..
West North Central States			
Minnesota	1	1	..
Iowa	4	4	1
Missouri	..	1	..
North Dakota	..	..	..
South Dakota	..	1	..
Nebraska	..	1	1
Kansas	..	..	..
South Atlantic States			
Delaware	..	..	..
Maryland	..	..	..
District of Columbia	..	..	..
Virginia	3	3	1
West Virginia	..	1	1
North Carolina	2	2	1
South Carolina	..	..	1
Georgia	..	..	..
Florida	3	3	..
East South Central States			
Kentucky	..	..	..
Tennessee	2	2	..
Alabama	1	2	..
Mississippi	3	4	1
West South Central States			
Arkansas	1	1	1
Louisiana	..	..	1
Oklahoma	..	2	1
Texas	4	5	9
Mountain States			
Montana	..	1	..
Idaho	..	..	..
Wyoming	..	..	..
Colorado	..	..	..
New Mexico	1	1	..
Arizona	1	2	..
Utah	..	..	..
Nevada	..	..	..
Pacific States			
Washington	..	..	..
Oregon	1	1	..
California	4	4	3
Alaska	..	..	..
Hawaii	..	..	1
Puerto Rico	..	..	3
Total	35	50	32

Psychiatrists Again Join Health Council.—The executive committee of the National Health Council by unanimous vote has reestablished the membership of the American Psychiatric Association in the council. The action followed a meeting of the council of the American Psychiatric Association on May 1, when it was voted to have the association reaffiliate with the health council. The move brought to 66 the membership of the council, which was established in 1921 and is composed of national organizations concerned with health improvement. Other recent additions to the membership of the council include the American Medical Association, the American College of Preventive Medicine, and the American Hospital Association.

Call for Papers on Goiter.—The fourth International Goiter Conference will be held at the Royal College of Surgeons, London, England, July 5-9, 1960. Abstracts of American papers to be considered for presentation should be sent to Dr. Joseph E. Rall, National Institute of Arthritis and Metabolic Disease, National Institutes of Health, Bethesda 14, Md. Abstracts from all other countries are to be sent to Dr. Selwyn F. Taylor, 3 Roedean Crescent, Roehampton, London, S. W. 3, England. All American abstracts must be received by Dr. Rall by Dec. 1. They should not exceed 400 words and should be submitted in quintuplicate. Presentation of papers will be limited to 15 minutes, and a copy of the final paper must be sent to the London Secretary two weeks prior to the meeting.

Meeting on Rehabilitation in Boston.—The 1959 national conference of the National Rehabilitation Association will be held at the Statler-Hilton Hotel, Boston, Oct. 26-28. The conference theme will be "Rehabilitation—A Positive Force." Among the topics to be presented by speakers and panel sessions are: The Impact of Medical Research on Rehabilitation, Progress of Medical Education and Rehabilitation, Rehabilitation Services for Children, Rehabilitation in Rural Areas, Structure of Federal and State Rehabilitation Agencies, the Disabled Person in the Home, the Responsibility of Insurance Carriers for Rehabilitation, the Influence of Emotional and Social Factors on Vocational Adjustment. There will be sectional meetings for persons interested in special areas of rehabilitation. Mr. Edward D. Callahan, Massachusetts Rehabilitation Commission, 14 Court Square, Boston 8, is serving as conference chairman.

Establish "Brain Bank" for Parkinson's Research.—The Parkinson's Disease Foundation, Inc., announced the establishment of a "brain bank" in its New York headquarters at 125 E. 50th St. Purpose of the "bank" is to make available the brains of deceased Parkinson's disease sufferers to "internationally renowned neurologists" and other experts engaged in scientific research projects of the Parkinson's Disease Foundation. Mr. William Black, president of the foundation, conceived the idea for establishing the "brain bank" after Mrs. Samuel Lewis, of New York City, donated the brain of her late husband to the foundation. The foundation is asking Parkinson patients who wish to donate their brains posthumously to this scientific research, to communicate their intention to the New York office. Thereafter the foundation will undertake all details and expenses involved in making the material available to scientists working in this field. The Parkinson's Disease Foundation has financially supported training fellowships and scientific research projects in 10 universities and two hospitals.

Graduate Study for Therapists.—The American Physical Therapy Association has received a grant from the U. S. Office of Vocational Rehabilitation to administer 15 traineeships of $2,400 each for graduate study for physical therapists. Purpose of the program is to assist the association in its efforts to increase the supply of physical therapists qualified by experience and graduate study for teaching, research, or "other positions of leadership." Eligibility requirements include membership in the American Physical Therapy Association; a baccalaureate degree from a regionally accredited college or university; a minimum of two years of experience in the clinical aspects of physical therapy; U. S. citizenship or a lawful admittance for permanent residence. Recipients of other federal benefits are ineligible. Additional requirements include acceptance by the graduate school of choice, evidence of physical and mental health, and a proposed, full-time program of study, leading to an advanced degree, related to administration, supervision, teaching, research, or clinical work. For information, write the American Physical Therapy Association, 1790 Broadway, New York 19.

Fellowship in Pulmonary Physiology in France.—A fellowship in pulmonary physiology for foreign doctors, particularly those from the United States is again available at the Pulmonary Physiology Laboratories of the University of Nancy Medical Center, Nancy, France, under the direction of Dr. Paul Sadoul, associate professor, University of Nancy School of Medicine. This fellowship commences October, 1959, or in 1960. It is for at least six months, preferably longer. It requires a cursory knowledge of the French language. It pays a bourse, or stipend, of about 40,000 francs per month and offers reasonable eating facilities at the university restaurants and possibly some type of lodging under la Cité Université, which costs about 10,000 francs per month. The work consists of both pulmonary function examinations on patients and experimental research work on animals in a newly constructed basic science building. The town of Nancy is in the province of Lorraine and closely situated to the borders of Germany, Belgium, Luxembourg, Holland, and Switzerland. For information, write directly to Dr. Paul Sadoul, Experimental Pathology Laboratory, 20 rue Lionnois, Nancy, France.

Report on Mental Hospital Admissions.—Mental hospital rolls showed a slight drop at the end of 1958, continuing a three-year downward trend, but at the same time, admissions to these hospitals rose sharply, the National Association for Mental Health said in its annual report. Resident patients in state and county mental hospitals numbered 545,000 on Dec. 31, 1958, compared with 548,000 at the end of 1957, a reduction of about one-half of one per cent. Admissions in 1958 were 210,000 compared with 195,000 in 1957—a rise of about 8%. The report remarked that of the 228 mental hospitals and institutions inspected according to minimum standards by the American Psychiatric Association by the end of 1958, only 34 were approved. Sixty-six had been given only conditional approval and 109 were disapproved. Reports on the remaining 19 had not yet been released. Other developments during 1958 included in the report were the increase in the number of community mental health clinics during the year, "primarily as a result of the operation of statewide Community Mental Health Acts," and the rise in federal government appropriations for research, training, and community services. Congress appropriated 52 million dollars for the budget of the National Institute of Mental Health, compared with 37 million in 1957.

Health Departments Win Sanitation Awards.—Salt Lake City and San Diego received highest awards for sanitation programs conducted by their health departments in a competition open to more than 1,200 local health departments throughout the country. Presentations were made at the annual meeting of the Western Branch, American Public Health Association, by Dr. Berwyn F. Mattison, executive director of the American Public Health Association. In the competition, sponsored by the Public Health Committee of the Paper Cup and Container Institute, the Salt Lake City (Utah) Health Department was judged first for "outstanding achievement in the development of a program for environmental sanitation" and the San Diego (Calif.) County Health Department was judged first for "outstanding achievement in the development of a program for eating and drinking sanitation." Dr. Mattison presented plaques to Dr. Richard J. Nelson, Salt Lake City's health commissioner, and Dr. Sidney B. Clark, San Diego County's assistant director of public health, for the achievements of their departments. For their personal leadership in the winning programs, bronze medallions were awarded to Dr. Nelson, Dr. Julius B. Askew, San Diego's director of public health, Mr. Wilbur C. Parkinson, Salt Lake City's director of environmental sanitation, and William B. Walshe, chief of San Diego's Division of Sanitation. A special certificate of merit was awarded to the Albuquerque (N. M.) Health Department for the excellence of its programs in both divisions of the contest—environmental sanitation and eating and drinking sanitation. The awards are made in memory of Dr. Samuel J. Crumbine, former executive officer of the Kansas State Board of Health and consultant to the Public Health Committee, Paper Cup and Container Institute.

FOREIGN

Congress of Nephrology in Geneva.—The first International Congress of Nephrology will be held Sept. 3-5 in Geneva and Evian under the presidency of Prof. R. Mach, of Geneva. Subjects for the congress will include the following: Regulation of Tubular Ionic Exchange; Pathologic Anatomy of the Kidney in Shock; Mechanism of Renal Lesions During Shock; and Clinical, Biologic and Therapeutic Aspects of Acute Renal Insufficiency Following Shock. The official languages will be French and English, with translation available during plenary sessions. A prize of 500,000 francs offered by the Societé des Eaux D'Evian will be awarded during the congress to the research worker less than 40 "who has made an important contribution to nephrology." Registration fees are $40 for active members, $28 for auxiliary members, and $10 for independent members. For information write: Dr. Gabriel Richet, Hotel Necker, 149 Rue de Sevres, Paris 15.

EXAMINATIONS AND LICENSURE

MEDICAL SPECIALTY BOARDS

American Board of Anesthesiology: *Written.* Various locations, July 8, 1960. Final date for filing application is January 8. Sec., Dr. Forrest E. Leffingwell, 217 Farmington Ave., Hartford 5, Conn.

American Board of Dermatology: *Written.* Several Cities, Oct. 5. *Oral.* Oklahoma City, Jan. 15-18, 1960. The final date for filing all applications is July 1, 1959. Sec., Dr. Beatrice M. Kesten, One Haven Ave., New York 32.

American Board of Internal Medicine: *1959 Schedule—Written,* Oct. 19. Final date for filing application was May 1. *Oral.* For candidates on the West Coast, Portland, Ore., Sept. 9-12. Final date for filing application was March 1. *Oral.* For candidates on the East Coast, Nov. 6-7, 9-10. Final date for filing application was March 1. Sec.-Treas., Dr. William A. Werrell, One West Main St., Madison 3, Wis.

American Board of Neurological Surgery: Examination given twice annually, in the spring and fall. In order to be eligible a candidate must have his application filed at least six months before the examination time. Sec., Dr. Donald D. Matson, 300 Longwood Ave., Boston, Mass.

American Board of Obstetrics and Gynecology: Applications for certificates, new and reopened, Part I, and requests for re-examination Part II are now being accepted. All candidates are urged to make such application at the earliest possible date. Deadline date for receipt of applications is August 1, 1959. No applications can be accepted after that date. Sec., Dr. Robert L. Faulkner, 2105 Adelbert Road, Cleveland 6, Ohio.

American Board of Ophthalmology: *Oral.* St. Louis, Oct. 6-10. Written. January 1960 in various cities. Applications for the 1960 written examination must be filed before July 1. Sec., Dr. Merrill J. King, Box 236, Cape Cottage Branch, Portland, Maine.

American Board of Orthopaedic Surgery: *Part II.* Chicago. Jan. 19-21, 1960. The deadline for the receipt of application is Aug. 15, 1959. Sec., Dr. Sam W. Banks, 116 South Michigan Ave., Chicago 3.

American Board of Otolaryngology: *Oral.* Chicago, Oct. 5-9. Final date for filing application was April 1. Sec., Dr. Dean M. Lierle, University Hospitals, Iowa City.

American Board of Pathology: New Orleans, Nov. 12-14. Final date for filing application is October 1. Sec., Dr. Edward B. Smith, Indiana University Medical Center, 1100 W. Michigan St., Indianapolis 7.

American Board of Pathology: *Examination in Forensic Pathology.* New Orleans, Nov. 13. Final date for filing application is October 1. Sec., Dr. Edward B. Smith, Indiana University Medical Center, 1100 W. Michigan St., Indianapolis 7.

American Board of Pediatrics: *Written.* January 1960. Exec. Sec., Dr. John McK. Mitchell, 6 Cushman Road, Rosemont, Pa.

American Board of Plastic Surgery: *Oral and Written.* Miami, Fla., Oct. 15-17. Final date for submitting case reports is July 1. Corresponding Secretary, Miss Estelle E. Hillerich, 4647 Pershing Ave., St. Louis 8, Mo.

American Board of Proctology: *Oral and Written.* Philadelphia, September. Final date for filing application was March 15. Sec., Dr. Stuart T. Ross, 520 Franklin Ave., Garden City, N. Y.

American Board of Psychiatry and Neurology: Chicago, Oct. 19-20; New York, Dec. 14-15; San Francisco, Mar. 14-15, 1960. Training credit for full time psychiatric and/or neurologic assignment in unapproved military programs or services between the dates of Jan. 1, 1950 and Jan. 1, 1954 was terminated on Jan. 1, 1959. Sec., Dr. David A. Boyd, 102-110 Second Ave. S. W., Rochester, Minn.

American Board of Radiology: *Examination.* Washington, Dec. 6-9. Deadline for filing application is July 1. Candidates examined in Diagnostic Roentgenology may expect to be examined in Physics. A Special Examination in Nuclear Medicine (for diplomates in Radiology or Therapeutic Radiology) was not given in June 1959. Candidates desiring this examination will be accommodated at the meeting of the Board in Washington, D. C. on December 5. Deadline for filing application is August 1. Sec., Dr. H. Dabney Kerr, Kahler Hotel Bldg., Rochester, Minn.

American Board of Surgery: *Written* examinations (Part I) will be held on December 2, 1959 at various centers to be announced later. Candidates are urged to apply several months before completion of training requirements although the closing date for filing applications is August 1. Those completing training requirements after September 30 cannot be considered for the Part I examination in December of the same year. Sec., Dr. John B. Flick, 1617 Pennsylvania Blvd., Philadelphia 3.

Board of Thoracic Surgery: *Written.* Various centers throughout the country, September 1959. Final date for filing application is July 1. *Oral.* September. Final date for filing application is July 1. Sec., Dr. William M. Tuttle, 1151 Taylor Ave., Detroit 2, Mich.

American Board of Urology: *Written.* Approximately 25 cities throughout the country, December 4, 1959. *Oral-Clinical* and *Examination in Pathology.* Chicago, February 1960. Final date for filing application is Sept. 1, 1959. Sec., Dr. William Niles Wishard, 30 Westwood Rd., Minneapolis 26, Minn.

GOVERNMENT SERVICES

AIR FORCE

Dr. Lamb Honored.—Dr. Lawrence E. Lamb, head of the department of internal medicine at the Air Force School of Aviation Medicine, received the Dr. Arnold D. Tuttle award at a meeting of the Aeromedical Association in Los Angeles in May. The honor is bestowed annually for achievement in aeromedical research and is accompanied by a bronze plaque and $500.

Medical Officers Honored.—Col. Harold V. Ellingson, director of education and plans, and Col. Lawrence J. Milch, chief, department of pharmacology-biochemistry, were awarded Air Force Commendation medals by Major Gen. Otis O. Benson Jr., commandant of the School of Aviation Medicine at Randolph Air Force Base, Texas, in May.

Dr. Stembridge Awarded Legion of Merit.—Dr. V. A. Stembridge was presented the Legion of Merit in May. He is associate professor of pathology at Southwestern Medical School in Dallas, Texas. He received the award for meritorious service as chief of the aviation pathology section of the Armed Forces Institute of Pathology during the period Feb. 11, 1956, to Jan. 15, 1959, while on active duty as a major in the United States Air Force Medical Service. His exemplary leadership and ceaseless efforts were instrumental in the Armed Forces Institute of Pathology attaining a position of world leadership as a reference center for the study of aviation fatalities.

Personal.—Major Gen. Otis O. Benson Jr., commandant of the Air Force School of Aviation Medicine at Randolph Air Force Base, Texas, was named president of the Pan American Medical Association's section of space medicine. He will head the section on space medicine at the association's congress, to be held in Mexico City next year.

Col. Fratis L. Duff, commander of the facility at Gunter Air Force Base, Ala., was awarded an Oak Leaf Cluster to his Legion of Merit, in June. The citation states, in part: "Under his command, the Gunter branch of the School of Aviation Medicine has furnished independent duty medical technicians for duty at isolated sites throughout the world; conducted an aviation physiological training center for USAF and allied students and major aircraft corporations on the principles of the partial pressure suit, and activated, trained and sent to overseas areas many specialized epidemiological flights."

ARMY

Personal.—On June 1, Col. Charles O. Bruce joined the staff of the department of professional services of the American Hospital Association, working primarily with the Committee on Infections. Colonel Bruce retired from the Army where his last assignment was chief of the department of epidemiology, Walter Reed Army Institute of Research.——Lieut. Col. Douglas Lindsey was named director of medical research of the Chemical Warfare Laboratories at Army Chemical Center in Maryland. He succeeds Col. Albert R. Dreisbach, who assumed command of the United States Army Hospital at Fort Monmouth, N. J. In addition to directing Army research on medical aspects of chemical warfare, Colonel Lindsey will serve as chemical warfare adviser to the Army Medical Research and Development Command.

NAVY

Navy Doctors Honored.—At the meeting of the Aerospace Medical Association in Los Angeles, in April, Capt. Clifford P. Phoebus, Medical Corps, U. S. Navy, received the Theodore C. Lyster award for outstanding achievement in the general field of aviation medicine; Capt. Edward L. Beckman, Medical Corps, U. S. Navy, was presented the Eric Liljencrantz award with its $500 honorarium for the best paper on basic research in the problem of acceleration; and Capt. Ross B. Lautzenheiser, Medical Corps, U. S. Navy, Capt. F. Kirk Smith, Medical Corps, U. S. Navy, and Capt. John T. Smith, Medical Corps, U. S. Navy, were elected Fellows of the Association for their outstanding contributions in the field of aviation medicine. At the same meeting Capt. Oran W. Chenault, Medical Corps, U. S. Navy, assistant chief of the Bureau of Medicine and Surgery for Aviation Medicine, was elected first vice-president of the association for fiscal year 1960. He will be president-elect in 1961 and president in 1962.

VETERANS ADMINISTRATION

Foster Homes for Mental Patients.—Placement of recovering mental patients in foster homes is giving the Veterans Administration the equivalent of a 1,500-bed mental hospital. The agency's foster home program, started in 1951, allows recovering mental patients to live in a home environment as a step in their return to the community. About 1,550 patients from its mental hospitals lived with "adopted" families in private homes near the hospitals in 1958, a 24% increase over the figure for 1957. The hospitals placed 807 patients in the homes in 1958 and reported 328 of those in the program recovered sufficiently to be discharged from hospital rolls.

DEATHS

Amick, Charles Leonard Ⓜ Wakarusa, Ind.; University of Louisville (Ky.) Medical Department, 1911; past-president of the Elkhart County Medical Society; veteran of World War I; on the staff of the Elkhart (Ind.) General Hospital and the Goshen (Ind.) General Hospital, where he died April 5, aged 74.

Anello, Vincent, Brooklyn; Columbia University College of Physicians and Surgeons, New York City, 1921; in 1954 created a Knight of St. Gregory by Pope Pius XII for his services to Roman Catholic charities; chief of medicine, St. Catherine's Hospital; died April 20, aged 63.

Barber, Walter Lewis Ⓜ Waterbury, Conn.; University and Bellevue Hospital Medical College, New York City, 1907; veteran of World War I; at various times president and secretary of the Waterbury Medical Association; fellow of the American College of Surgeons; member of the honorary staff in surgery and past-president of the medical staff, Waterbury Hospital, where he died April 10, aged 78.

Beall, Ira Washington Ⓜ Libertytown, Md.; College of Physicians and Surgeons, Baltimore, 1893; on the emeritus staff of the Frederick (Md.) Memorial Hospital, where he died April 16, aged 91.

Beard, James Randolph Ⓜ Newark, N. J.; born in Summerville, S. C., Dec. 5, 1903; Cornell University Medical College, New York City, 1929; served on the faculty of his alma mater; joined the medical staff of the Mutual Benefit Life Insurance Company in 1946, becoming medical director in 1948; veteran of World War II; member of the Association of Life Insurance Medical Directors of America; for nine years served on the Passaic township committee and at various times served as mayor and police and fire commissioner; served on the staff of the Bellevue Hospital in New York City; president of the board of trustees of the Florence Crittenden League; died in Millington April 14, aged 55.

Blasdel, Harry E. Ⓜ Hutchinson, Kan.; Washington University School of Medicine, St. Louis, 1921; veteran of World War I; on the staffs of the Grace Hospital and St. Elizabeth Mercy Hospital, where he died April 5, aged 64.

Bowns, William James, Carmichael, Calif.; University of Southern California School of Medicine, Los Angeles, 1956; interned at the Orange County General Hospital in Orange, Calif.; member of the courtesy staff, Sutter General Hospital; died in the Sutter Memorial Hospital March 26, aged 44.

Bull, David Chapman Ⓜ New York City; Columbia University College of Physicians and Surgeons, New York City, 1916; specialist certified by the American Board of Surgery; served on the faculty of his alma mater; in 1916 served on the Mexican border with United States Cavalry; veteran of World War I; decorated with the Purple Heart and the Silver Star; for many years associated with the Columbia-Presbyterian Medical Center; founder of the Blood Transfusion Association; died April 18, aged 66.

Butler, Alfred Worcester, Chatham, Mass.; Tufts College Medical School, Boston, 1923; veteran of World Wars I and II; died in the Naval Hospital, Chelsea, April 6, aged 64.

Byfield, Arthur Frederick Ⓜ Ephraim, Wis.; Rush Medical College, Chicago, 1907; specialist certified by the American Board of Internal Medicine; veteran of World War I; served on the faculty of Northwestern University Medical School in Chicago, where he was associated with the Passavant Memorial Hospital; served on the staff of the Highland Park (Ill.) Hospital; died in St. Petersburg, Fla., April 22, aged 77.

Casey, Frank Joseph, Omaha; Creighton University School of Medicine, Omaha, 1924; veteran of World War I; on the staff of St. Catherine's Hospital, where he died April 3, aged 63.

Cottingham, Carl Parvin, Uniontown, Ky.; University of Louisville (Ky.) Medical Department, 1904; served as president of the Uniontown Farmers Bank; died in St. Mary's Hospital, Evansville, Ind., April 7, aged 76.

Daniel, Bluefort C., Hogansville, Ga.; Atlanta Medical College, 1895; in 1955 Hogansville honored him by holding a "Dr. Daniel Day"; died in the City-County Hospital in LaGrange April 3, aged 87.

Davis, Walter William Ⓜ Chester, N. Y.; born in Syracuse Jan. 7, 1880; Syracuse University College of Medicine, 1903; served on the Chester Board of Education for 10 years and was president for six; since 1936 school physician; for many years village health officer; served as president of the Orange County Medical Society; member of the New York State Health Officers Association and the New York State School Health Officers Association; served as consultant in medicine at Tuxedo Me-

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Ⓜ Indicates Member of the American Medical Association.

morial Hospital in Tuxedo Park, where recently he received an honorary appointment in that capacity; served on the board of managers of the Estelle and Walter C. Odell Memorial Sanatorium in Newburgh; for many years associated with the Goshen (N. Y.) Hospital, where he died April 13, aged 79.

Deubel, Harry Francis, Hamilton, Ohio; University of Cincinnati College of Medicine, 1927; formerly county coroner; served as county physician; on the staff of the Mercy Hospital; died April 8, aged 61.

Hartrick, Louis Eugene, Champaign, Ill.; Northwestern University Medical School, Chicago, 1910; also a graduate in pharmacy; died in the Mercy Hospital, Urbana, March 19, aged 81.

Head, Marvin Monroe Ⓜ Zebulon, Ga.; Atlanta College of Physicians and Surgeons, 1902; past-president of the Medical Association of Georgia; veteran of World War I; for many years mayor of Zebulon and member of the county board of education; served on the board of commissioners of Pike County; surgeon for the Southern Railway for over fifty years; associated with Griffin-Spalding County Hospital in Griffin and the Upson County Hospital in Thomaston; on the board of directors of the Bank of Zebulon; died March 31, aged 78.

Holland, Arthur Lawrence Ⓜ New York City; New York University Medical College, New York City, 1897; fellow of the American College of Physicians; consulting physician, New York Infirmary; gastroenterologist, New York Hospital; consulting physician at the Mount Vernon (N. Y.) Hospital and the Elizabeth A. Horton Memorial Hospital in Middletown; died Jan. 20, aged 85.

Hooker, John Williams Ⓜ Danville, Va.; born in Wausau, Wis., Aug. 9, 1914; Northwestern University Medical School, Chicago, 1939; certified by the National Board of Medical Examiners; specialist certified by the American Board of Pathology; member of the College of American Pathologists and the American Society of Clinical Pathologists; served as president of the Pathological Society of Virginia; assistant in clinical pathology, Bowman Gray School of Medicine in Winston-Salem, N. C.; at one time professor of pathology at the Hahnemann Medical College in Philadelphia; formerly practiced in Wilmington, Del., where he was on the courtesy staffs of St. Francis, Wilmington General, and Delaware hospitals; on the staff of the Memorial Hospital; died in the North Carolina Baptist Hospital in Winston-Salem, N. C., April 2, aged 44.

Hoxie, George Howard Ⓜ Berkeley, Calif.; born in South Easton, N. Y., July 24, 1872; Universität Zürich Medizinische Fakultät, Switzerland, 1901; specialist certified by the American Board of Internal Medicine; fellow of the American College of Physicians; member of the Endocrine Society; served as president of the Missouri Tuberculosis Association; formerly practiced in Kansas City, Mo., where he was on the staffs of the Kansas City General, Research, and St. Luke's hospitals, and served as medical director of the public schools; from 1902 to 1905 associate professor of anatomy and professor of medicine from 1905 to 1911 at the University of Kansas School of Medicine, Kansas City, where from 1905 to 1911 he was dean of the clinical department; died in the Herrick Memorial Hospital, Berkeley, April 10, aged 87.

Hudnall, Richard Llewellyn, Lilian, Va.; Barnes Medical College, St. Louis, 1904; for many years served on the county board of supervisors; died April 5, aged 81.

Huggard, Timothy Stephen Ⓜ Oglesby, Ill.; Chicago College of Medicine and Surgery, 1909; veteran of World War I; member of the staffs of St. Margaret's Hospital in Spring Valley and Peoples Hospital in Peru; member and past-president of the staff at St. Mary's Hospital in La Salle, where he died March 17, aged 78.

Johnson, Ben Frank Ⓜ Mondovi, Wis.; Marquette University School of Medicine, Milwaukee, 1923; veteran of World War I; health officer; associated with Sacred Heart Hospital in Eau Claire and the Buffalo Memorial Hospital; died March 17, aged 67.

Katz, Samuel David Ⓜ University City, Mo.; University of Wisconsin Medical School, Madison, 1929; specialist certified by the American Board of Pathology; member of the American Society of Clinical Pathologists; on the staff of Faith Hospital in St. Louis; died March 16, aged 51.

Kimball, Melvin Clinton Ⓜ Borger, Texas; University of Oklahoma School of Medicine, Oklahoma City, 1931; member of the American Academy of General Practice; past-president of the Hutchinson County Tuberculosis Association; on the staff of the North Plains Hospital, where he died March 24, aged 51.

Kleiman, David Ⓜ Raleigh, N. C.; University of Illinois College of Medicine, Chicago, 1935; past-president of the Raleigh Mental Health Association; veteran of World War II; on the staffs of Rex, St. Agnes, and Mary Elizabeth hospitals; died in the Rex Hospital March 28, aged 48.

Kosse, James Ⓜ Chicago; Albertus-Universitat Medizinische Fakultat, Konigsberg, Prussia, 1937; for many years associated with the Veterans Administration; veteran of World War II; died April 10, aged 47.

Kracaw, Forest Charles Ⓜ Oakland, Calif.; Marquette University School of Medicine, Milwaukee, 1916; specialist certified by the American Board of Otolaryngology; associated with the Oakland Naval Supply Center; died April 6, aged 67.

Krause, George Lynn Ⓜ St. Louis; University of Pennsylvania School of Medicine, Philadelphia, 1925; fellow of the International College of Surgeons and the American College of Surgeons; formerly police surgeon; associated with St. Luke's Hospital and the Missouri Baptist Hospital; since 1932 district surgeon for the Cotton Belt Railroad; since 1949 surgeon for the Carter Carburetor Corporation; died March 23, aged 61.

Kusmin, Harry, Cleveland; University of Pittsburgh School of Medicine, 1912; died March 23, aged 70.

Lamon, Goldson Test, St. Petersburg, Fla.; University of Pennsylvania Department of Medicine, Philadelphia, 1892; served as president of the Westmoreland County (Pa.) Medical Society; for many years practiced in New Kensington, Pa., where he was on the staff of the Citizens General Hospital; died in the Bayou Sanitarium March 28, aged 88.

Learn, Blair George Ⓜ Blandburg, Pa.; Jefferson Medical College of Philadelphia, 1920; past-president of the Clearfield County Medical Society; veteran of World War I; died in the Altoona (Pa.) Hospital April 4, aged 67.

Little, Charles Francis Ⓜ Great Falls, Mont.; Creighton University School of Medicine, Omaha, 1921; fellow of the American College of Physicians, served as president of the Great Falls Heart Association; on the staffs of the Columbus and Montana Deaconess hospitals; died in Denver March 19, aged 67.

McIntire, Landon Rolla Ⓜ St. Charles, Mo.; Washington University School of Medicine, St. Louis, 1933; president of the school board; veteran of World War II; on the staff of St. Joseph Hospital; died April 2, aged 50.

McKillop, Gordon Lovejoy Ⓜ Gaylord, Mich.; University of Western Ontario Faculty of Medicine, London, Ont., Canada, 1924; member of the American Academy of General Practice; a charter member and past-president of the local Kiwanis Club; chief of staff, Otsego County Memorial Hospital, where he died March 24, aged 64.

McMillen, Arch Stinson, Fort Dodge, Iowa; University of Nebraska College of Medicine, Omaha, 1934; associated with St. Joseph Mercy and Lutheran hospitals; member of the American Society of Clinical Pathologists and the Radiological Society of North America; past-president of the Iowa Radiologists Association and past-secretary of the Iowa Association of Pathologists; died March 24, aged 50.

Macer, Clarence Guy Ⓜ Evansville, Ind.; Northwestern University Medical School, Chicago, 1912; on the staffs of the Deaconess, St. Mary's, and Welborn Baptist hospitals; died March 24, aged 73.

Maercklein, Adolph Gustave, Ellendale, N. D.; Wisconsin College of Physicians and Surgeons, Milwaukee, 1902; medical examiner for the draft board during World War I; served as mayor of Ellendale; for many years superintendent of health for Dickey County; died March 16, aged 80.

Martinez, Roman Daigre Ⓜ Plaquemine, La.; Medical Department of Tulane University of Louisiana, New Orleans, 1909; immediate past-president of the Sixth District Medical Society; veteran of World War I; for many years Iberville Parish coroner; president of the Plaquemine Sanitarium; charter member and first president of the Plaquemine Lions Club; died March 29, aged 71.

Meyersohn, Franz Ⓜ Worcester, Mass.; Friedrich-Wilhelms–Universitat Medizinische Fakultat, Berlin, Prussia, 1915; on the medical staff at the Jewish Home for Aged for many years; a courtesy staff physician at the Memorial and Hahnemann hospitals; died in the Worcester City Hospital March 20, aged 68.

Moran, Noel Dunbar, Versailles, Ind.; Indiana University School of Medicine, Indianapolis, 1935; member of the American Academy of General Practice; Ripley County coroner two terms; a member of the staff of Margaret Mary Hospital at Batesville and Decatur County Memorial Hospital at Greensburg; past-president of Versailles Lions Club; died at Mardel Hunting Reserve in Trimble County, Ky., March 15, aged 56.

Morrow, Rufus Ethel, McKinney, Texas; Memphis (Tenn.) Hospital Medical College, 1904; honorary member staff, Collin Memorial Hospital; died in the Richardson Hospital, Jasper, March 26, aged 81.

Musman, Samuel, Lynn, Mass.; Middlesex College of Medicine and Surgery, Waltham, 1933; veteran of World War II; died March 18, aged 49.

Nacey, Lawrence James Ⓜ Rochester, N. Y.; Queen's University Faculty of Medicine, Kingston, Ontario, Canada, 1913; specialist certified by the American Board of Otolaryngology; member of the American Academy of Ophthalmology and Otolaryngology; served overseas during World War I; for many years served as otologist for the city public schools;

on the staff of the Hospital of State Agriculture and Industrial School in Industry; associated with St. Mary's Hospital; died March 26, aged 73.

Nast, Jerome Ⓜ Corpus Christi, Texas; University of Pennsylvania School of Medicine, Philadelphia, 1919; member of the American Academy of General Practice; past-president of the Nueces County Medical Society; veteran of World War I; associated with Spohn and Memorial hospitals; died in the Spohn Hospital March 20, aged 63.

Nebeker, William Marcellus Ⓜ Salt Lake City, Utah; Northwestern University Medical School, Chicago, 1926; specialist certified by the American Board of Obstetrics and Gynecology; associate clinical professor of obstetrics and gynecology at the University of Utah College of Medicine; veteran of World War I; for ten years chairman of the medico-legal committee of the Utah Medical Association; on the staffs of the Latter Day Saints and Holy Cross hospitals; died March 28, aged 61.

Nelson, George Osborne Jr., North Attleboro, Mass.; Columbia University College of Physicians and Surgeons, New York City, 1943; interned at Boston City Hospital; certified by the National Board of Medical Examiners; veteran of World War II; medical director of Union Carbon and Carbide Company; died March 25, aged 40.

Nelson, Robert James Ⓜ Clinton, Iowa; State University of Iowa College of Medicine, Iowa City, 1926; interned at the Grace Hospital in Detroit; veteran of World War I; past-president of the Clinton County Medical Society; associated with Jane Lamb Hospital and the St. Joseph Mercy Hospital, where he died March 13, aged 62.

Nevin, John Lewis Ⓜ San Bernardino, Calif.; State University of Iowa College of Medicine, Iowa City, 1918; fellow of the American College of Surgeons; associated with St. Bernardine's Hospital and the San Bernardino County Charity Hospital, where he was at one time assistant superintendent; died April 7, aged 67.

Newson, Howard Egbert Ⓜ San Anselmo, Calif.; University of California School of Medicine, San Francisco, 1926; associated with St. Francis Memorial and Mary's Help hospitals in San Francisco; died March 21, aged 65.

Niblock, George Frederick Ⓜ Derby, Iowa; College of Physicians and Surgeons of Chicago, School of Medicine of the University of Illinois, 1900; died in Royal Center, Ind., April 4, aged 87.

O'Leary, Daniel W. Ⓜ Norman, Okla.; University of the South Medical Department, Sewanee, Tenn., 1904; died March 24, aged 85.

Owen, Henry Isaac, Canton, Ill.; Barnes Medical College, St. Louis, 1901; for many years practiced in Fulton, Mo., where he served as city physician and as resident physician at the Missouri School for Deaf; veteran of World War I; died in Peoria March 22, aged 83.

Paolillo, Charles Gerald Ⓜ New Britain, Conn.; Yale University School of Medicine, New Haven, 1935; interned at New Britain General Hospital; certified by the National Board of Medical Examiners; secretary of the staff at New Britain Memorial Hospital and a member of the staff of New Britain General Hospital; died March 24, aged 50.

Patten, Vernon Cole Ⓜ Morristown, Ind.; University of Indianapolis Medical Department, 1897; veteran of World War I; died March 29, aged 88.

Peter, William Wesley, Port Republic, Md.; born in Elliston, Ohio, Dec. 1, 1882; Rush Medical College, Chicago, 1910; for years engaged in public health work in China; one of the founders and the director of the China Council on Health Education, with which he served from 1911 to 1926; visiting lecturer at Pennsylvania St. John's University Medical School, Shanghai, from 1920 to 1926 and the Peking Union Medical School, from 1920 to 1926; during World War I served with the Chinese Labor Corps in France; upon his return to America joined the staff of the American Public Health Association as associate secretary; when the Cleanliness Institute in New York was established in 1927, became its health consultant, and in 1929 director of the health service, serving until 1933; the following year appointed medical director for the Navajo Indian Reservation, with headquarters at Albuquerque, N. Mex.; resigned as associate professor of public health and chief of sanitary inspection in the department of health, Yale University School of Medicine in New Haven, Conn., in 1945 when he became director of the training division of the Institute of Inter-American Affairs, Washington, D. C.; professorial lecturer of public health, George Washington University, Washington, D. C., 1945-1949; specialist certified by the American Board of Preventive Medicine; in 1927 received his doctor of public health from Yale; died in the National Institutes of Health in Bethesda, March 31, aged 76.

Pilgram, Ralph Edward Ⓜ Paxtang, Pa.; Hahnemann Medical College and Hospital of Philadelphia, 1917; served in France during World War I; formerly member of the school board; at one time county health officer; died in Harrisburg March 22, aged 69.

Pilkington, Albert Ⓜ Newton Square, Pa.; Medical College of Virginia, Richmond, 1900; died in Burn Brae Hospital, Clifton Heights, Feb. 5, aged 85.

Pote, Thomas B. Ⓜ St. Louis; Washington University School of Medicine, St. Louis, 1902; for many years lecturer in pathology at his alma mater and associated with the U. S. Bureau of Animal Industry; died March 30, aged 91.

Powers, Lunette I. Ⓜ Muskegon, Mich.; Northwestern University Woman's Medical School, Chicago, 1897; member of the American Academy of General Practice; on Nov. 10, 1947, was honored at a dinner by Muskegon County doctors who served overseas during World War II; they presented her a plaque with the inscription, "To Lunette Powers for her efforts in helping us to keep our morale in war service"; in 1950 named by the Michigan State Medical Society as "Michigan's Foremost Family Physician"; served on the staffs of the Mercy and Hackley hospitals; died March 24, aged 83.

Prey, Duval Ⓜ Denver; University of Colorado School of Medicine, Denver, 1922; member of the founders group of the American Board of Surgery; member of the Western Surgical Association; fellow of the American College of Surgeons; associated with St. Joseph's, St. Luke's, Presbyterian, Mercy, and Denver General hospitals; died Feb. 6, aged 62.

Quinn, Robert Edward Ⓜ Hanover, N. H.; Yale University School of Medicine, New Haven, Conn., 1950; interned at the Walter Reed General Hospital in Washington, D. C.; served a residency at the Mary Hitchcock Memorial Hospital in Hanover, Veterans Administration Hospital in White River Junction, Vt., and the Peter Bent Brigham Hospital in Boston; specialist certified by the American Board of Internal Medicine; certified by the National Board of Medical Examiners; instructor in medicine at Dartmouth Medical School since 1956; associated with the Veterans Administration Hospital in White River Junction, Vt., and the Mary Hitchcock Memorial Hospital; attached to the military service from 1950 to 1952; died in February, aged 32.

Rizzo, Frank Michael Ⓜ Sibley, Iowa; Loyola University School of Medicine, Chicago, 1941; interned at Iowa Methodist Hospital in Des Moines; associated with the Osceola Hospital; died March 28, aged 50.

Robinson, G. W., Prairie View, Ark. (licensed in Arkansas in 1903); died March 19, aged 85.

Seely, Alvane Cary, Roseburg, Ore.; Medical College of Ohio, Cincinnati, 1893; specialist certified by the American Board of Otolaryngology; past-president of the state board of health; past-president of the Douglas County Medical Society; served as county health officer, member of the city council, president of the Chamber of Commerce, and president of the Rotary Club; on the staff of the Mercy Hospital; designated examiner for the Veterans Administration Hospital; died March 21, aged 89.

Shelly, James Acuff, Ambler, Pa.; University of Pennsylvania School of Medicine, Philadelphia, 1917; veteran of World War I; served as burgess of Ambler; associated with the Chestnut Hill Hospital in Philadelphia and the Abington (Pa.) Memorial Hospital, where he died April 9, aged 67.

Shepard, Cassius Marion Ⓜ Columbus, Ohio; Jefferson Medical College of Philadelphia, 1899; at one time member of the school board; member of the American Academy of Orthopaedic Surgeons; fellow of the American College of Surgeons; for many years on the staff of the Grant Hospital; died in St. Anthony's Hospital March 24, aged 87.

Siebert, Walter Joseph Ⓜ St. Louis; Washington University School of Medicine, St. Louis, 1926; specialist certified by the American Board of Pathology; member of the American Society for Experimental Pathology; served on the faculty of his alma mater; formerly on the staff of St. Joseph Hospital in Alton, Ill., and De Paul Hospital in St. Louis; associated with the Lutheran Hospital, in St. Louis, St. Elizabeth Hospital in Belleville, Ill., St. Francis Hospital in Washington, Mo., and St. Joseph Hospital in Highland; died March 13, aged 59.

Sorter, Alfred Ⓜ New York City; Medizinische Fakultät der Universität, Vienna, Austria, 1922; served on the staffs of the Mount Sinai and Medical Arts hospitals; died March 31, aged 63.

Stambul, Joseph Ⓜ Philadelphia; Temple University School of Medicine, Philadelphia, 1920; author of "The Mechanisms of Disease"; associated with Albert Einstein Medical Center, Southern Division, where he died April 11, aged 67.

Stanton, Edwin MacDonald Ⓜ Duanesburg, N. Y.; born in 1879; University of Pennsylvania Department of Medicine, Philadelphia, 1903; member of the founders group of the American Board of Surgery; member of the American Association of Obstetricians and Gynecologists; life member and past-governor of the American College of Surgeons; president for two years of the Schenectady Bureau of Municipal Research; president in 1946 of the Schenectady Chamber of Commerce; a member of the city planning commission many years and its chairman two years; a director of the Schenectady Trust Company; consultant, Ellis and St. Clare's hospitals in Schenectady; received the Merit Award of the Iowa State College; died in the Mayo Clinic, Rochester, Minn., April 9, aged 79.

Stanze, Frank J. Ⓜ St. Louis; St. Louis College of Physicians and Surgeons, 1909; member of the American Academy of General Practice; associated with St. Anthony's Hospital and Alexian Brothers Hospital, where he died April 6, aged 78.

Stephenson, Samuel Logan Sr. Ⓜ Corinth, Miss.; Memphis (Tenn.) Hospital Medical College, 1909; veteran of the Spanish-American War, Boer War, and World War I; associated with Corinth and Community hospitals; formerly practiced in Marks, where he was health officer of Quitman County; died in Campbell's Clinic April 6, aged 77.

Stone, Fordyce Homer Ⓜ Beulah, Mich.; Hering Medical College, Chicago, 1911; associated with the Paul Oliver Memorial Hospital in Frankfort and the James Decker Munson Hospital in Traverse City; director of the Central State Bank in Beulah; died April 2, aged 71.

Stroud, Ernest Jeffrey Ⓜ Jonesboro, Ark.; University of Tennessee College of Medicine, Memphis, 1934; interned at the City Hospital in Cleveland; fellow of the American College of Surgeons; past-president of the Craighead-Poinsett Counties Medical Society; chief of surgery at St. Bernard's Hospital, where he served as vice-chief of medical staff; vice-president of Citizens Federal Savings and Loan Association; died in the Baptist Memorial Hospital, Memphis, Tenn., March 18, aged 51.

Sullivay, Rosa Lee Ⓜ Pensacola, Fla.; Maryland Medical College, Baltimore, 1912; died April 4, aged 82.

Taylor, Charles Benjamin Ⓜ Oklahoma City, Okla.; Georgetown University School of Medicine, Washington, D. C., 1905; veteran of World War I; medical director of the state department of welfare; past-president of the Oklahoma City Academy of Medicine; served on the faculty of the University of Oklahoma School of Medicine, where in 1949 an annual lectureship was established in his honor; died April 7, aged 79.

Telford, Alexis T. Ⓜ Olney, Ill.; Missouri Medical College, St. Louis, 1896; formerly county coroner; served on the staff of the Richland Memorial Hospital; at one time member of the staff of the State Asylum Hospital, Chester; died in Crown Point, Ind., April 6, aged 86.

Teller, Ernest Ⓜ Chicago; Medizinische Fakultät der Universität, Vienna, Austria, 1926; member of the American College of Chest Physicians and the American Trudeau Society; clinical assistant professor of medicine, the Chicago Medical School; on the staff of Mount Sinai Hospital; chief of tuberculosis control, Illinois Department of Public Welfare; died April 10, aged 57.

Tepper, Abram Samuel Ⓜ Far Rockaway, N. Y.; University and Bellevue Hospital Medical College, New York City, 1913; specialist certified by the American Board of Pediatrics; served overseas during World War I; formerly president of the Rockaway Medical Society and the Queens Pediatric Society; associated with St. Joseph's Hospital, where he was president of the medical board and director of pediatrics; for 40 years served as physician to the Hebrew Kindergarten and Infants Home; died April 14, aged 67.

Vaughan, Robert Renwick Ⓜ McConnell, W. Va.; Chattanooga (Tenn.) Medical College, 1906; past-president of the Logan County Medical Society; served on the staff of the Holden (W. Va.) Hospital; died in Logan (W. Va.) General Hospital April 2, aged 78.

Wagner, Gordon Thomas Ⓜ West Richfield, Ohio; Western Reserve University School of Medicine, Cleveland, 1939; interned at St. Vincent Charity Hospital in Cleveland, where he served a residency; veteran of World War II; fellow of the American College of Surgeons; on the staff of the Medina (Ohio) Community Hospital; died April 5, aged 46.

Ward, John William Ⓜ Plumsteadville, Pa.; University of Pennsylvania School of Medicine, Philadelphia, 1932; a member of the county board of health; on the staffs of the Doylestown (Pa.) Hospital and Abington (Pa.) Memorial Hospital; a director of the Doylestown (Pa.) National Bank; died April 14, aged 53.

Ware, Fritz Lee, Warrenton, Ga.; University of Georgia Medical Department, Augusta, 1914; died in Augusta March 30, aged 74.

Warren, Charles Bowen Ⓜ Gill, Colo.; College of Physicians and Surgeons, Baltimore, 1894; died March 24, aged 93.

Warshaw, Arthur Harry, Torrance, Calif.; University of Kansas School of Medicine, Kansas City, Kan., 1931; veteran of World War II; died April 7, aged 52.

Wenzell, Albert Gould Ⓜ Captain, U. S. Navy, retired, La Mesa, Calif.; Georgetown University School of Medicine, Washington, 1915; entered the U. S. Navy in 1919 and retired Oct. 1, 1937; veteran of World War II; died April 4, aged 68.

White, Benjamin Lewis, St. Petersburg, Fla.; Atlanta College of Physicians and Surgeons, 1912; died March 2, aged 71.

Williams, Clyde Lewis Ⓜ Linesville, Pa.; Medical Department of the Western University of Pennsylvania, Philadelphia, 1897; veteran of World War I; served on the staff of the Spencer Hospital in Meadville; died in Palm Springs, Calif., March 4, aged 66.

FOREIGN LETTERS

AUSTRIA

Absenteeism.—At the meeting of the Society of Physicians in Vienna on March 27, Dr. C. Frieberger stated that, on the basis of the records of the Social Insurance Funds, it has been established that the Austrian national economy in the years between 1951 and 1955 lost a yearly average of 28,600,000 working days, or about 5% of the total work days of the employed. The national income, which amounted to 102 billion schillings in 1956, could therefore have been larger by over 5 billion schillings, had no working days been lost through illness. Of the illnesses causing time lost from work 25% were due to accidents and 25% to colds and gastrointestinal diseases. Many of these illnesses could have been prevented.

Lymphogranuloma and Pregnancy.—At the same meeting Dr. G. Brichta and co-workers reported that, of 92 women who had been treated for lymphogranuloma at the second medical clinic of the University of Vienna, 8 were so treated during pregnancy. In most patients lymphogranuloma is not made worse by pregnancy, although in some an exacerbation of the lymphogranulomatosis may occur in the course of pregnancy. Transmission of the disease from mother to child through the placenta appears to have been confirmed by critical examination in only a single case collected from the world literature. Treatment of lymphogranulomatosis during pregnancy consists, in addition to general supportive measures, in the local use of x-rays and possibly the administration of cortisone.

Influenza.—At the same meeting Dr. Henneberg of Berlin stated that only under particular circumstances will it be possible to include in an influenza vaccine the specific strain responsible for a given epidemic. A variant that is predominant for a while disappears after the population has had wide exposure to it. A new strain may not be suitable in all cases for the manufacture of a vaccine, or the manufacturing of a suitable vaccine may come too late in the course of an epidemic. Since many viruses cause influenza-like diseases of the respiratory tract, evaluation of the success of a vaccine against influenza is difficult in the individual case and can be made only in the presence of an epidemic.

BRAZIL

Carcinoma of the Cervix.—Dr. H. Stoltz, of the Institute of Gynecology, Rio de Janeiro National University (*An: brasil. ginec.* 47:125, 1959), analyzed the records of the first 10,000 consecutive patients attending the Cancer Detection Center of the Institute, where, since 1948, colpocytology and colposcopy have been used routinely. Biopsy is performed whenever a neoplasm is suspected or atypical tissues, yellow thickened mottled mucosa, leukoplakia, areas of atypical transformation, or erosion of the cervix are observed. All polyps of the cervix are excised, and curettage of the uterus is performed on all patients who report acyclic or postmenopausal bleeding.

Patients whose colposcopic findings were questionable and whose colpocytological findings were not had their lesions reexamined under magnification and special illumination, and a local treatment of the inflammatory process was started. Small areas of mottling inside a zone of transformation were considered questionable and the decision to get a biopsy specimen was suspended until the cytological findings were known. In those patients whose colpocytological findings were questionable and whose colposcopic findings were not the examination was repeated. In a few patients with diffuse or hemorrhagic colpitis on the first examination a great improvement was observed after a week, and a questionable area of mucosa was noticed that had been previously masked by the colpitis. In such patients biopsy should be performed. If the biopsy specimen is negative, local treatment is recommended to help determine the diagnosis. Vaginal applications of a sulfonamide or antibiotic and the local and parenteral use of hormones is tried.

It is thus usually possible to make a definite diagnosis within a few weeks. Owing to the long latency of intraepithelial carcinoma of the cervix this delay does not endanger the patient's life. The interpretation of the histological preparations is not always easy. The pathologist sometimes says "suspected invasive lesion" or "carcinoma," when a minute lesion seen at colposcopy was totally extirpated by the biopsy. These difficulties can be overcome by a close cooperation between the colposcopist, who has an exact knowledge of the topography of the lesion, and the pathologist, who interprets the histological aspect. To cut the specimen block in another direction sometimes clarifies the diagnosis.

The items in these letters are contributed by regular correspondents in the various foreign countries.

This plan permitted the discovery, in the entire series of 10,000 patients, of 60 patients with intraepithelial carcinoma of the cervix stage 0, 13 with microcarcinomas, and 38 more with carcinoma stage 1, who, although not suspected at the first clinical examination, could later have their lesions correctly diagnosed by colposcopy and biopsy. As more and more women were examined at the center the rate of cases of invasive carcinoma diminished and more young patients were attended, thus proving that, in the last years of the decade, all the hospitalized patients had had the advantage of a routine examination and an early diagnosis. Intraepithelial carcinoma of the cervix can now be discovered in asymptomatic patients. Every gynecologic service should give all patients the benefit of colposcopic and colpocytological examinations and make histological studies of all questionable lesions. The diagnosis may be difficult during pregnancy and in the presence of inflammatory processes, but prolonged observation during the treatment should clarify the diagnosis.

Measurement of the Pressure and Flow of Bile.—Dr. P. L. Castelfranchi, of the medical school of Ribeirão Preto City (São Paulo State University), stated that, besides the known causes of trouble in peroperative manometry of the bile ducts such as the preoperative use of drugs and anesthetics, the introduction of foreign bodies in the ducts and changes in intraabdominal pressure added to the unreliability of currently used methods for such measurement (*Rev. paulista med.* 54:123, 1959). Some of these methods (Bove's, Horta's, Mallet-Guy's, and Rose's) subject the biliary ducts to unphysiological tensions. Caroli's roentgenographic manometry, which is free from these objections, uses for contrast an irritant liquid and requires a cumbersome and highly specialized equipment. Moreover, all methods but Horta's fail to measure the biliary flow, which, from the standpoint of changes in the extrahepatic ducts, is much more important than the pressure itself. In Horta's apparatus, which measures the flow by taking account of the number of centimeters of linear fall of a physiological saline solution, each centimeter corresponds to 1 ml. of bile. The bile is not secreted under constant pressure.

Castelfranchi's equipment includes (1) a flask to hold 1,000 ml. of a saline solution; (2) a phleboclysis dropper, modified by the introduction of two lateral electrodes; (3) an electronic counter connected to the electrodes; (4) two pieces of latex tubing; (5) a curved metal cannula; (6) a water manometer inserted between the two pieces of tubing by means of a T-shaped metal tube at the bottom; and (7) a fixed vertical support to hold the flask of solution at an adjustable height. The distinctive features of this new apparatus are the saline solution flask and the modified dropper. The great capacity of the flask prevents the flow of a small amount of solution from influencing the preestablished level of the hydrostatic pressure. The electronic connections permit a count of the drops as they intermittently close the circuit. The apparatus is calibrated by means of the falling drops, the number of which indicates the flow of bile in milliliters per unit of time.

Amebiasis.—At a meeting of the Medical Academy of São Paulo Amaral and Pires, of the University of São Paulo, reported that they had treated 10 patients who had amebiasis with beta-oxy-nitrobenzil-dichloracetamide (Mebinol). The patients had few if any symptoms attributable to their amebiasis. Each patient received 500 mg. of the drug three times a day for 10 days. All were cured and the drug was well tolerated. Before and after the treatment (1) formed stools from all patients were examined by the method of Faust and that of Hoffman, Pons, and Janer, and (2) stools after a dose of sodium sulfate were stained with iron and hematoxylin. The authors recommend this scheme of fecal examination for evaluation of the results of treatment because it reveals practically all the carriers in a group, and there are practically no false-negative results.

Chronic Urethritis.—At a meeting of the Saint Luke's Medical Society of São Paulo in May Dr. G. V. de Azevedo analyzed a series of 150 patients with urethritis, 120 of whom were women and 30 of whom were girls. Proliferations of the exterior urethral meatus were found in 11.6% and of the interior duct in 33.3% of the adult patients. More than 90% of both adults and children were cured. Neisseria gonorrhoeae was the causative organism in less than 50%. The route of the infection was ascending, descending, lymphogenic, or hematogenic. Proliferations occurred frequently, either inside the duct (pseudopolyps and small cysts) or in the external orifice (caruncles, polyps, or papillomas). Care must be taken to differentiate these lesions from carcinoma. The disease is characterized by the following cycle: pain, emptying of the bladder, relief from pain, and return of pain with refilling of the bladder. Cystourethroscopy is an important aid to diagnosis. Treatment consists of eliminating the causative focus of infection and such local measures as progressive dilation, combined with instillation of drugs and fulguration or electrocoagulation.

The Use of Tourniquets.—In the January-February issue of *Revista do Hospital das Clinicas,* Dr. L. B. de Abreu examined the advantages and disadvantages of the use of the pneumatic tourniquet for temporary hemostasis in injuries to the hand. He concluded that the pneumatic tourniquet when properly used offers great advantages to both patient and surgeon, with little risk even when used for a prolonged period. Nonpneumatic tourniquets, such as rubber tubes and Esmarch bandages, however, may cause irreparable damage even when used for a few minutes.

FINLAND

Test for Rheumatoid Arthritis.—J. Kirpilä (*Acta rheumatol. scandinav.* 4:276-285, 1958) made intracutaneous Congo red tests on 115 patients with rheumatoid arthritis. Their color reactions were found to be greater than those of 30 normal persons, and the color took longer to disappear in members of the diseased group. Tests made on the back and thigh were clearer in these respects than those made on the volar and dorsal surfaces of the skin of the arm. There was no asymmetry. The intensity of color and the rate of disappearance depended on the degree of severity of the disease. The rate of disappearance was slower in younger persons. To simplify the testing process the author recommended that it be made only on the skin of the thigh. The result then need not be read for the first time until the 4th day, and the next reading can be left until the 10th or 12th day.

Reduction of Radiation Dose.—Reductions in the radiation dose to the gonads have been achieved by combining different factors. C.-E. Johanson-Unnérus and co-workers (*Ann. med. int. Fenniae* 48:71-80 [supp. 28] 1959) made a comparative study of 180 women. Bearing in mind that obstetric examinations and hysterosalpingographies constituted a relatively great hazard to the human genes, their aim was to reduce the gonadal dose received in these examinations. The results showed that with use of high-speed film, rapid screens, added refiltration, higher kilovoltage, and lowered amperage it was possible in routine work to reduce the total gonadal dose in obstetric examinations from 0.3 to 0.04 r. In connection with hysterosalpingographies the corresponding reduction was from 2.27 to 0.54 r.

Metastatic Thyroid Carcinoma.—Holsti and Rytilä (*Ann. med. int. Fenniae* 48:35-49 [supp. 28] 1959) treated 14 patients who had metastatic thyroid carcinoma with radioiodine (I^{131}). Of these 11 were subjected to only partial thyroidectomy. In eight of them the uptake of I^{131} was observed in the metastases, although a portion of normal thyroid tissue was present. Of these two were follicular, one alveolar, two adenopapillary, one adenomatous, and one anaplastic carcinoma, and one was a malignant adenoma. Of the negative cases one with follicular carcinoma and one with adenomatous carcinoma showed uptake after the first therapeutic dose of I^{131}, one adenomatous carcinoma showing negative results to the end. In several patients success was achieved in arresting metastatic growth with I^{131}. The largest total dose was 405 mc. Even after partial thyroidectomy it was possible in some patients to create conditions which promoted successful treatment with I^{131}. Of the 14 patients treated with I^{131} 8 showed satisfactory results, some of them in combination with x-ray therapy. Four patients died, and the treatment of one was still in progress. The best results were achieved in patients with follicular carcinoma. Complications were rare. Transient falls in the leukocyte and platelet counts were noted. Two patients developed radiation sialadenitis after administration of 153 and 405 mc., respectively. Excretion of I^{131} through the salivary glands was highest in hyperthyroid patients. Two women of child-bearing age were treated, but neither had any disorders of menstruation. One of them received 45 mc. because of metastases in the cervical lymph nodes and the other 85 mc. because of pulmonary metastases.

Pyruvic Acid Concentration and Carcinoma.—The blood pyruvic acid concentration in 82 patients suffering mainly from gynecologic carcinoma was studied by Järvinen and Widholm (*Ann. med. int. Fenniae* 48:81-88 [supp. 28] 1959). Part of the investigation concerned the treatment of hyperpyruviemia with vitamin B_1 derivatives. The series included 31 patients with cervical carcinoma whose blood pyruvic acid concentrations were determined prior to treatment, after each three applications of radium, and after x-ray therapy. The blood pyruvic acid concentration was slightly higher in patients with carcinoma than in the control series. It rose during radium therapy to a peak after the third radium application. It fell somewhat after roentgenotherapy but was still slightly higher at the end than before the treatment. The authors assumed this to be due either to the greater degree of decomposition of carcinoma tissue containing pyruvic acid during radium therapy, whereby great quantities of partly anaerobically decomposed substances pass into the blood, or to the effect of some kind of stress.

Twenty-three patients with gynecologic carcinoma at some phase of their treatment after the disappearance of radiation intoxication symptoms were given a five-day course of 100 mg. of cocarboxylase intravenously per day. Cocarboxylase lowered the blood pyruvic acid concentration. In all the patients a favorable clinical effect on the intoxication symptoms was demonstrable. The remaining 28 patients, including 6 with nongynecologic carcinoma, were given 240 mg. of thiamine intramuscularly per day after the appearance of radiation intoxication symptoms. This agent also lowered the blood pyruvic acid concentration and had a clinically beneficial effect on the patients' general conditions. In most patients the treatment effected an increase in the leukocyte count, which had decreased during radiation therapy. The authors concluded that the use of cocarboxylase and thiamine was beneficial in patients who because of the hyperpyruviemia caused by radiation intoxication were unable to tolerate the continuation of the lifesaving radiation therapy. It was not necessary to discontinue radiation therapy in any of these patients.

Left-sided Gallbladder Without Situs Inversus.—Transposition of the gallbladder to the left side of the median line without situs inversus is rare. O. Kuosmanen (*Ann. med. int. Fenniae* 48:160-166 [supp. 28] 1959) described two patients, a man and a woman aged 34 and 35, respectively, in whom a left-sided gallbladder without situs inversus was diagnosed in the first roentgenographic examination. In one of them there was a floating gallbladder which moved to the right side in connection with the contraction produced by an egg meal. The author emphasized the necessity of examining the left side of the abdomen either by fluoroscopy or roentgenography in connection with cholecystography in patients in whom the gallbladder shadow was not visualized in the customary cholecystograms of the right side. An erroneous conclusion that the contrast medium did not enter the gallbladder might otherwise be reached. Although this condition is rare, when it does exist its preoperative diagnosis is important.

Radiotherapy for Inoperable Cancer.—M. Koulumies (*Ann. med. int. Fenniae* 48:145-152 [supp. 28] 1959) reported a series of 262 patients with inoperable cancer of the breast. Of these 225 received radiotherapy but in 37 the treatment had to be restricted to the administration of appropriate drugs. Of the patients treated with irradiation 20 were alive after five years, 10 of these being free of symptoms. When all inoperable patients were considered 8% were alive after five years, 4% being clinically free of symptoms. Of another series of 181 patients with inoperable cancer of the breast 4 patients or 2% were alive after 10 years. These patients were free of symptoms. Although the results of treatment in patients with inoperable cancer of the breast are comparatively poor as far as a final cure is concerned, irradiation, particularly in locally inoperable cases, may bring about freedom from symptoms for 5, 10, or even 20 years. The fact should also be appreciated that by this treatment these patients may enjoy a temporary improvement, sometimes of several years' duration, and amelioration of their symptoms.

While x-ray treatment of intrathoracic metastases from carcinoma of the breast has generally been regarded as hopeless, Koulumies and Sarajas-Kyllönen in the same issue reported that 92 patients with carcinoma of the breast received x-ray treatment for intrathoracic metastases at the Helsinki Institute of Radiotherapy in the period 1938 to 1956. Of this number 38 improved and 2 became free of symptoms. In patients treated with larger doses of radiation the results were definitely better than the average for the total series. Of the 33 patients in whom a dose of 4,000 r was used on the breast tumor 19 improved and 2 became asymptomatic, and these patients also survived longer after radiation to the metastases. In this series of 92 patients the survival period was longer than that of the patients in the control group whose intrathoracic metastases were not treated with radiation. A number of patients in both series had undergone castration by x-rays or hormones. Even though therapy resulted in improvement or freedom from symptoms as far as a particular metastasis was concerned, it was found that other metastases developing elsewhere might be beyond the reach of therapeutic measures. With x-ray treatment of intrathoracic metastases from carcinoma of the breast the authors relieved the sufferings of these patients and delayed the progress of this chronic disease.

Carcinoma of Lungs.—O. Peräsalo and co-workers (*Ann. med. int. Fenniae* 48:228-236 [supp. 28] 1959) studied the results of operation in patients with carcinoma of the lung. Of 870 such patients 323 were operated on. The operative mortality was 14%, and it was twice as high in patients over 60 years of age as in younger persons. About 30% of the patients survived one year, 25% two years, 23% three years, 20% four years, and 13% five years. The five-year survival rate was highest in the group with adenocarcinoma and lowest in the patients with squamous cell carcinoma. The series also included all cases of curative resection. Restriction of the tumor to the lung appeared to be the most important circumstance influencing prognosis. In patients surviving five years or more the tumor had not extended outside the lung into surrounding structures; two of these had received postoperative radiotherapy.

Radiophosphorus and Cancer.—Because of their elevated metabolism carcinomatous and sarcomatous tissues have a greater affinity for radiophosphorus (P^{32}) than normal tissue, and this fact may be used in the diagnosis of tumors. Tala and Lieto (*Ann. med. int. Fenniae* 48:289-295 [supp. 28] 1959) studied the P^{32} uptake in 10 patients (2 with carcinoma of the breast, 1 with metastases in the axillary nodes, 2 with metastases in the thoracic wall, 4 with endobronchial carcinoma, and 1 with sarcoma of the femur). Beta activity was counted from the tumor and from the corresponding point on the other side of the body. In the patients with carcinoma of the lung the counting was performed with a miniature Geiger counter inserted through a bronchoscope. In eight histologically confirmed malignant tumors the ratio of impulses at the point of measurement to that at the control point was 1.3:1 or higher. In two patients in whom the tumor was situated at a depth of more than 8 mm. from the Geiger tube the ratio was 1:1. Beta rays emitted by phosphorus have a limited depth of penetration of 8 mm., and inflammatory changes may produce an elevated phosphorus metabolism. Degeneration of cancer cells may also cause a depressed phosphorus metabolism. The use of P^{32} in the diagnosis of malignant tumors is of value in patients in whom the tumor may be reached by the counter.

Postmortem Observations on Tumor Diagnoses.—Teir and Koivuniemi (*Ann. med. int. Fenniae* 48: 296-309 [supp. 28] 1959) analyzed 768 autopsy reports which indicated that tumors were found. The clinical diagnosis was verified by autopsy in 556 cases, or 72.5%. Metastasis had been diagnosed clinically but the primary site of tumor remained undetermined in 11 cases, or 1.4%. Malignant disease had been diagnosed but the primary site was incorrect in 53 cases, or 6.9%. In 32 cases, or 4.2%, malignant disease had been diagnosed but the tumor was unspecified. There were 116 tumors (15.1%) which eluded any clinical diagnosis. The average degree of accuracy (72.4%) was exceeded in the groups of tumors of the blood and bone marrow, 94%; breast, 93%; male genital organs, 90%; and respiratory system, 78%. Most important among the groups that remained below the average degree of accuracy were the tumors of the digestive organs, 55%. In the cases of tumors of the pancreas 29% had been clinically diagnosed.

Hodgkin's Disease.—Voutilainen and Saxén (*Ann. med. int. Fenniae* 48:323-338 [supp. 28] 1959) reported a series of 120 patients (73 men and 47 women) with Hodgkin's disease or malignant lymphogranulomatosis. The biopsy slides of 77 of them were examined but 10 had to be discarded. In this verified series the five-year survival rate was 22% and in the total series 21%. The average survival from the start of treatment was 2.1 years. When the symptoms prior to admission were also considered the five-year survival rate in both series was about 31%. Of the 67 patients whose biopsy slides were studied 3 were entirely free of symptoms. In these treatment had been started at an early stage, and the patients survived for five, seven, and nine years respectively. The most important factor influencing the prognosis was early institution of therapy when the clinical features were involvement of a single lymph node region.

The dose of radiation should be sufficient for destruction of the lymphatic involvement. The best results were obtained in the age group from 21 to 40 years. Patients with more advanced cases and constitutional symptoms should also first receive roentgenotherapy and later medication, or both. Women withstood the treatment better and generally lived longer than men; 40% of the women having involvement of two or more lymph node regions in both the upper and lower trunk, with other constitutional symptoms such as occasional fever, anemia, or pruritus, survived over five years. From the histological findings the survival rate may be predicted with fair accuracy. Hodgkin's sarcoma responded most poorly to treatment, whereas cases showing chiefly the changes of reticular lymphoma were more benign. A high degree of fibrosis was a good prognostic sign. For the best results the authors recommended that treatment be started early when a single lymph node region is involved and that treatment should be intensive. Periodic checking is important in the later stages. Prophylactic irradiation of the cervical lymph nodes is recommended.

FRANCE

Mongolism.—In spite of numerous researches on Mongolism, a congenital disease that afflicts about one of every 800 live infants, its origin has been obscure. Dr. J. Lejeune and co-workers have discovered, by means of cultures of connective tissue, a chromosomal aberration in victims of Mongolism. At a meeting of the National Academy of Medicine they reported that they observed in 10 children with this condition the constant presence of a small supernumerary chromosome with a terminal kinetochore in the form of a V. This is the first time a chromosomal origin of a disease of human beings has been reported.

Myocardial Infarction.—At the same meeting Poumailloux and Viart reported studies on the frequency of myocardial infarctions in relation to solar and geomagnetic activities. In the periods Jan. 17-22 and Sept. 1-3, 1957, they observed several cases of myocardial infarction and found that there was an increase in solar activity between Jan. 17 and 25, with maximal magnetic agitation on Jan. 21, and also between Aug. 28 and Sept. 3, with maximal magnetic agitation on Sept. 2. In 1958 they noted an increased incidence of myocardial infarctions between March 21 and 30, Nov. 16 and 21, Dec. 4 and 6, and Dec. 15 and 17. They found that there was exceptionally great solar activity between March 20 and April 2, between Nov. 15 and 17, strong geomagnetic activity on Dec. 2 and 4, and between Dec. 10 and 17 several strong chromospheric eruptions with average intensity of solar spots but very strong geomagnetic activity on the 13th and 17th. It would seem from these observations that coronary accidents often occur one or two days after periods of vigorous geomagnetic activity.

GERMANY

Hydroxydione.—Investigations by D. Franke and co-workers (*Anaesthesist*, vol. 8, 1959) confirmed the useful qualities of hydroxydione in anesthesia. Induction is smooth and no side-effects were observed. Blood circulation and coagulation were unaltered. Electroencephalograms showed an initial pattern similar to that of normal sleep followed by longer periods of "black-out." A definite disadvantage was the lack of an antidote. Such analeptics as bemegride are not true antidotes. In some hypertensive patients a fall in blood pressure but no other circulatory disturbance was observed. A definite place may be assigned now to hydroxydione in the anesthetic armamentarium, but particular attention must be given to the dosage. The danger of phlebitis is best overcome by a rapid intravenous injection of a concentrated solution at body temperature, followed by injection of saline solution.

Freeze-drying Human Milk.—The usual technique of freeze-drying human milk has had restricted use, because it required milk of low bacterial count for safe storage. In more than half the collected samples the bacterial count proved to be higher than the accepted maximum of 50,000 per ml., despite all precautions. Friedberg and Steinheuer from the University of Mainz (*Deutsche med. Wchnschr.* 84:792, 1959) have overcome this limitation by heating the milk to 100 C for three hours after freeze-drying. This reduces the bacterial count to a survival rate of less than 0.01%. Prolonged storage (one or two months) reduces the bacterial count even further. Electrophoretic analysis of the protein pattern showed that the composition of the milk remained essentially unchanged with this treatment, the enzymatic activity of alkaline phosphatase being reduced by 4 to 20%, that of lactic dehydrogenase by 50%, and that of glutamic oxalacetic transaminase by 35%. No significant loss of biological activity was demonstrable, even after two years' storage at room temperature and after transportation. The milk was used successfully in the feeding of premature babies and those with severe gastroenteritis.

Serologic Tests in Blood Grouping.—According to P. Dahr many small hospitals perform ABO and Rh blood-grouping and crossmatching tests before transfusions incorrectly (*München. Med. Wchnschr.* 101:803, 1959). This fact becomes evident during law suits resulting from deaths after blood transfusions. Donors of the blood group O are not always suitable as universal donors. Blood from a donor of group O is dangerous if anti-A or anti-B antibodies are present in a high titer in the serum. Crossmatching must be performed before every transfusion, even when the recipient has previously tolerated blood from the same donor. It should also be performed in emergency cases where the results cannot be read before the transfusion is started. In some cases crossmatching can be supplemented by the indirect antiglobulin method. The physician performing a blood transfusion is responsible for the correct interpretation of the blood-grouping tests in the recipient as well as for the crossmatching. This responsibility must, however, be shared by the laboratory technicians actually making the tests.

Diabetic Coma in Children.—A special kind of diabetic coma was observed in six children by Krainick and Tittmann from the children's clinic of the University of Freiburg (*Arch. Kinderh.* 159:15, 1959). Characterized by a high-grade ketoacidosis and only a moderate hyperglycemia this kind of coma is of special interest both therapeutically and pathogenetically. The patients show a strong tendency to develop ketosis, resulting in frequent relapses into coma. Because of the resistance to insulin, treatment with this drug, in contrast to the treatment of hyperglycemic coma, will aggravate the ketosis unless dextrose is also given—preferably by continuous intravenous infusion. Alkalinization and cocarboxylase are also used in treatment.

Massive Gastric Hemorrhage.—According to Hoffmann and Kingreen of the University of Cologne (*München med. Wchnschr.* 101:532, 1959) in most of their series of 109 patients with massive gastric hemorrhage the bleeding originated from a peptic ulcer. In most cases the diagnosis is not difficult. In patients with arterial hemorrhage if the diagnosis can be made or assumed by the rapid loss of blood, resection should be performed within the first few hours. Preliminary treatment of several days to allow subsidence of the sequelae of shock is of value if the patient's condition permits. This must be decided by a careful clinical observation. The age of the patient is an important factor. All 10 persons who died without being operated on were over the age of 45. Of the 63 patients discharged from the hospital 36 were over 45. In patients with hemorrhagic gastritis the authors did not resect the stomach and none of these patients died.

Massive hemorrhage after partial resection or gastroenterostomy requires especial evaluation. In such patients the presence of a marginal ulcer of the anastomosis or of an old peptic ulcer must be clarified. The same general principles are valid as for the patient with a stomach not yet operated on. The ulcer is resected but the gastrojejunitis is conservatively treated. In patients with cancer, which seldom causes massive hemorrhage, resection should be performed. Each patient must be individually evaluated. In those with massive hemorrhage from esophageal varices conservative therapy is advisable, if necessary with the three-barrel balloon probe described by Sengstaken. After control of the hemorrhage operation should be considered.

Cardiac Insufficiency.—W. Busse and co-workers (*München. med. Wchnschr.* 101:407, 1959) treated 113 patients who had cardiac insufficiency with combinations of digoxin and theobromine or theophylline and adenosine. They obtained saturation with 3.75 mg. of digoxin given by mouth within five days. The full orally effective level was calculated at 2.63 mg. They obtained saturation with 2.85 mg. of digoxin given intramuscularly in five days. The intramuscular effective level was calculated at 1.95 mg. Compared with intravenous administration the loss by intramuscular administration amounted to about 12%. After saturation through either route the average oral maintenance dose was 0.41 mg. A standard administration of 0.75 mg. of digoxin daily until the onset of the full effect was a useful procedure. The origin of the cardiac insufficiency was not a decisive factor in determining the dosage. Patients with tachycardia should not be completely eliminated from consideration for this type of treatment.

Cortisone and Tuberculosis.—F. Schwandner (*München. med. Wchnschr.* 101:622, 1959) described two women in whom the severe activation of pulmonary tuberculosis was caused by cortisone therapy. Both patients gave a history of old inactive tuberculosis. In the first case the clinical examination should have been supplemented by a roentgenogram of the lungs, which would have led to detection of the pulmonary process. In the second a physical examination of the lungs had been omitted. The author therefore urged that before institution of cortisone therapy careful investigations should be made to discover inactive tuberculosis. If evidence of tuberculosis is found or even suspected, and if cortisone is indicated as it was in both patients here reported, cortisone should be applied only if the patient is under simultaneous protection with antibiotics.

Purpura Annularis.—Among those diseases characterized by extravasation of erythrocytes purpura annularis telangiectodes is only little known outside the field of dermatology. This disease, whose cause is unknown, belongs to the group of vascular hemorrhagic diseases. It can readily be differentiated from other forms of purpura by clinical, capillary microscopic, and histological criteria, according to K. W. Kalkoff (*München. med. Wchnschr.* 101:586, 1959). The histological characteristics are a lymphohistiocytic infiltrate, intracellular and extracellular deposits of hemosiderin, and absence of fibrin. A typical finding in the microscopy of the capillaries is an escape of erythrocytes around the intermediary links. The clinical findings include small dot-like petechiae (hemorrhages of the intermediary links), uniform focal erythema (dilatation or new formation of blood-vessels), formation of nodules (lymphohistiocytic infiltration), brownish pigmentation (hemosiderin deposits), eczema-like symptoms, and a tendency to central retrogression of lesions and simultaneous peripheral progession.

Smallpox.—In December, 1958, there was an outbreak of smallpox in Heidelberg which extended into January. In order to counteract exaggerated reports in the daily press, *Deutsche medizinische Wochenschrift* (no. 5, 1959) gave an accurate description of the outbreak. Smallpox was first observed in a doctor of the medical clinic of Heidelberg University who had returned from a journey to India early in December. On the return trip he contracted fever in Ceylon and flew back to Europe, while his wife returned by ship. The doctor returned to duty, but because of folliculitis he consulted a dermatologist. The skin manifestations at that time were not typical, but a diagnosis of smallpox was not excluded. Precautionary isolation was therefore recommended, and subsequent virologic examination confirmed the diagnosis. In the meantime the entire hospital staff and all patients were vaccinated, provided there were no contraindications. The clinic was closed to outsiders, and persons suspected of contact infection were isolated.

Complete quarantine was enforced after two contacts developed smallpox. The staff and patients of the other hospitals were also vaccinated, and the population of Heidelberg was advised to undergo precautionary vaccination. About 30,000 persons responded to the call. In all cases the infected persons had come in contact with the doctor who had returned from India. In some cases the contact was only a brief stay in the patient's room. Except in two patients the disease took a mild course, the so-called varioloid occurring in persons vaccinated many years earlier whose resistance had greatly diminished. Two patients died in spite of all medical care—a 70-year-old woman who had not been revaccinated since childhood and who suffered from a severe hepatic disease and a 26-year-old woman doctor in the clinic, never previously vaccinated because of allergic manifestations. Further spreading of smallpox through the contacts was prevented.

Tubular Insufficiency and Renal Failure.—Tubular insufficiency was considered by E. Wollheim of the University of Würzburg (*München. med. Wchnschr.* 101:597, 1959) as a uniform clinical syndrome characterized by slight excretion of protein, microhematuria, reduction of renal concentrating power, reduced excretion of phenol red, occasionally by renal epithelium in the urine, and rarely by cylindruria. All degrees of severity may be observed, from a normal quantity of urine to anuria, and during recovery there may be polyuria. In patients with severe tubular damage nitrogen retention increases excessively, and electrolyte imbalance may occur (especially hypopotassemia and hyperpotassemia).

Tubular insufficiencies are observed in patients with infectious diseases; allergies; circulatory disturbances; poisonings by mercury, carbon tetrachloride, or mushrooms; damage due to transfusion of incompatible blood; and renal ischemia or hypoxia due to vascular insufficiencies, shock, or hepatic or diabetic coma. Tubular insufficiencies remain anhypertonic, as long as the vascular apparatus of the glomeruli is not involved or as long as intrarenal pressure does not occur. Secondary tubular insufficiencies may occur as complications in patients with subacute or chronic glomerulonephritis. The tubular involvement can be diagnosed in these patients by the loss of concentrating power and the increase of residual nitrogen. It can be clearly distinguished from the nephroses with severe albuminuria and edema. The distinction of primary tubular from primary glomerular functional disorders is necessary for proper treatment. The term "tubular insufficiency" comprises all degrees of severity of tubular functional disturbances and therefore corresponds better to clinical reality than the term "acute renal failure."

INDIA

Uterine Hypoplasia.—Karande and Gajkhandh (*Journal of Obstetrics and Gynecology of India*, vol. 9, March, 1959) used estradiol benzoate to treat uterine hypoplasia. The study included 29 unselected patients with uterine hypoplasia, irrespective of their menstrual status. The uterine length was less than 8 cm. in all the patients and they were examined twice a week through at least one menstrual cycle. The uterine length was measured at each examination and cervical mucus was collected for study. Endometrial biopsy specimens were taken once a month, usually during the premenstrual phase. The authors injected 1 cc. of aqueous suspension containing 10 mg. of estradiol benzoate intracervically once a month at the beginning of the menstrual cycle. In patients with regular menstrual cycles a cyclic variation in uterine length was noticed, ranging from 0.2 to 1.2 cm. No such variation was found in patients with primary amenorrhea. The average variation before treatment with intracervical injections was 0.41 cm. and after treatment it was 0.85 cm. Each patient received an average of three intracervical injections. The maximum length of the uterus during a particular cycle was closely related to the type of menstrual cycle (anovulatory or ovulatory).

Endometrial biopsy studies in the premenstrual period showed secretory phase in 12 of the 29 patients and in these the maximum uterine length was present during the premenstrual phase in 10 and intermenstrual phase in 2 patients; 14 showed the proliferative phase in endometrial biopsy studies performed two or three days prior to the period. In all of these the maximum length was reached in the intermenstrual period. The three patients with primary amenorrhea who had no cyclic variation in length did not show any endometrium in biopsy specimens. Within four days of intracervical injection the length of the uterus increased by as much as 1.5 cm., but the effect started wearing off gradually within about 20 days and just before the next period the length was little more than that before injection. One patient with infrequent menses and scanty endometrium showed no enlargement of the uterus after intracervical injection. The effect of the injection on cervical mucus was observed in these 29 patients through 66 menstrual cycles. Of the 66 cycles 29 or 44% of the total showed a proliferative phase in the premenstrual period; 48% of these showed typical total crystallization and 41.3% partial crystallization of the cervical mucus just prior to the period. The amount of the mucus ran parallel to the changes in crystallization. All patients with anovulatory cycles should have total crystallization in the premenstrual period if the estrogen secretion is normal. Negative and partial crystallization in 41.3% and 10.3% of these patients, respectively, indicated deficient estrogen secretion.

Of the total number of cycles 40.9% were ovulatory, showing the secretory phase during the premenstruum; 74.07% of these showed no crystallization, 18.5% atypical crystallization, and 7.43% typical crystallization. Thus progesterone secretion was deficient in patients who showed total and atypical crystallization. In three patients the mucus was thick, dirty, and scanty throughout the menstrual cycle and showed no crystallization pattern. They showed the most striking response to intracervical injection of estradiol benzoate. Within four days of injection the mucus became transparent, increased in amount, and showed partial crystallization. This effect lasted for 20 to 25 days after which the mucus reverted back to its original condition. A beneficial effect of the injection was also seen in patients with anovulatory cycles and partial or atypical crystallization, but it was also transient. In ovulatory cycles the amount of mucus increased in the early but not the later part of the cycle. With the dosage and mode of administration used the injection did not alter the pattern of mucus crystallization in patients with ovulatory or anovulatory cycles.

JAPAN

Burn Scars and Cancer.—Drs. Ito and Fujimaka (*Acta Medica et Biologica*) reported a series of 13 patients with burn scars, biopsy specimens of which revealed cancer. The patients' ages ranged from 20 to 70 years. The elapsed time between the burn and the diagnosis of cancer averaged 38 years.

Carbon Monoxide Heart.—In a mountainous region north of Tokyo there is a farming community with a population of about 2,000 where rice and hemp are grown. Dr. Tomio Komatu, the local health officer, noticed that each spring about 33% of the inhabitants were afflicted with edema of the face and hands. Further questioning showed that they had chronic heart trouble, rheumatism, and beriberi. About 40% of the deaths in this region were from cardiac causes. Investigation revealed that in the winter these people worked processing hemp fibers in poorly ventilated rooms, heated with open charcoal fire boxes. The carbon monoxide concentration in the air under these conditions averaged 70 parts per million (ppm) and in some rooms reached 200 ppm. A concentration of 100 ppm is sufficient to provoke symptoms of acute carbon monoxide poisoning. The installation of stoves and closed heating systems brought about the complete disappearance of the symptoms, including dyspnea and palpitation, and the annual number of deaths in the region dropped from 65 to 7.

Trachoma.—Mikuni and Tsuchiya *(Acta Medica et Biologica)* stated that they observed a high percentage of cure in patients who had trachoma with the use of oxytetracycline, chlortetracycline, and chloramphenicol. More recently they used the latter alone to determine the optimum strength. With petrolatum used as a base they tried seven strengths ranging from 0.1 to 5.0%. The applications were made once a day and the patient was considered cured if the conjunctiva was restored to normal appearance and the granules and papillae completely disappeared. They found that the 2% preparation gave as good results as the stronger preparations. The lesser strengths were almost as effective but the treatment took a little longer. The average patient took eight weeks to get well. About 80% were cured and the rest markedly improved.

NORWAY

Cerebrovascular and Cardiovascular Disease.—Reports presented at a meeting of the Norwegian Medical Society in Oslo showed that the statistical handling of the data at present available with regard to deaths from cerebrovascular and cardiovascular disease tends to raise questions rather than answer them. Prof H. J. Ustvedt compared the mortality from cerebrovascular disease in Norway from 1927 to 1954 with that from cardiovascular disease in the age groups 40-59, 60-79, and 80 years and over. In the age group 40-59 the mortality from cardiovascular disease rose greatly for men in the postwar years, whereas there was no such rise for women of the same age at the same time. Another puzzling observation was that for men of this age group there was a marked rise in the mortality from cardiovascular disease but no such rise from cerebrovascular disease. Ustvedt had sought an explanation for these discrepancies in possible errors of diagnosis, registration, and classification but had been driven to conclude that they were real.

At the same meeting Dr. K. B. Osvik gave a statistical analysis of postmortem findings in 51 patients who had died so soon after admission to Ullevaal hospital that there had been no time for a proper clinical examination. Here cerebrovascular disease was found post mortem to be responsible for 16 deaths, myocardial infarct for 18, other heart disease for 13, and a variety of other ailments for the rest. Deaths from cardiac disease were predominant in patients under the age of 60 years and deaths from cerebral disease after this age.

Acute Depression and Iproniazid.—At the University Psychiatric Clinic iproniazid was given to 115 patients suffering from acute depression. Reporting on 100 of these A. Straand *(Tidsskrift for den norske laegeforening*, April 15, 1959) recommended a dosage of 50 mg. daily for three days with a gradual rise to 150 mg. daily thereafter, beyond which he did not go. In 43 patients a full remission was achieved. The drug had no beneficial effect in 56 patients, and one became worse. The drug had to be discontinued on account of side-effects in 10, and 20 complained of giddiness, unsteady gait, lassitude, a rapid pulse, and headache. The drug had, however, the merit of reducing the frequency with which shock treatments had to be given. From the patient's point of view it may be an attractive alternative to such treatment.

SWEDEN

Nonspecific Urethritis.—At the dermatological department of the Karolinska Hospital, Stockholm, treatment of nongonorrheal urethritis with penicillin and streptomycin has not, in the experience of Karltorp and Lodin, given very encouraging results. They have now (*Nordisk medicin*, March 19, 1959) approached the problem from another angle, having given tetracycline hydrochloride or tetracycline hexametaphosphate to ambulatory patients. Under bacteriological control 72 men between the ages of 20 and 30 were found to harbor Staphylococcus albus and/or various other organisms such as enterococci. The former drug was given to 29 and the latter to 26, the dosage for both being 500 mg. thrice daily for three days. Serving as controls were 17 men who received no drugs. Among the 29 were 23 men who were rid of their symptoms within five days, 4 who showed improvement, and 2 who were no better. Among the 26 were 23 who were rid of their symptoms within five days, 2 who showed improvement, and 1 who was no better. Among the

17 control patients only 1 was rid of his symptoms within five days, 7 showed some improvement, and 9 were no better. Neither of the drugs provoked any serious side-effects necessitating their discontinuance. Among the 72 patients were 28 with a history of gonorrhea and 7 with a history of nonspecific urethritis. In 29 the urethritis had been preceded by an infection of the upper respiratory tract. Several untreated patients showed a parallel abatement of the symptoms in the respiratory tract and the urethra. Of the two drugs the phosphate is to be preferred to the hydrochloride.

UNITED KINGDOM

Burden of Mental Hospitals.—A unified service for the aged infirm and sick would free mental hospitals from the incubus of largely incurable old people whose mental infirmity is such that they could be accommodated elsewhere, according to a booklet by Dr. C. P. Blacker, of Bethlehem Royal and Maudsley hospitals, London. By an unclogging of the mental hospitals the movements of patients would become freer and their management would be smoother. The interests of patients of all ages would be promoted, and many frustrations of doctors and administrators throughout the mental health service would be mitigated. Although persons over 65 years of age comprise only about 12% of the population, they occupy 32% of the beds in mental hospitals. The number of old and infirm persons is likely to increase in the next 30 years, and the already massive figure of 32% may swell to 40%.

Hospital and local health authorities should jointly coordinate the medical care available for the old and infirm. Policy should be decided by local groups of representatives of official and voluntary organizations. Appointment of an officer of health for the elderly, comparable to the children's officer now employed by local authorities, might assist in this coordination. He could act as secretary of the local group. The respect for the elderly which is so prevalent in the Orient is becoming rare in the industrialized West.

Hazards of Ships' Surgeons.—*The British Medical Journal* of April 18 commented on the legal position of the ship's surgeon in different countries. To practice as a doctor in Great Britain is hazardous enough, but the legal hazards facing the ship's surgeon are even greater. If a ship's surgeon has a mishap with a British passenger or a British seaman, at least the standards by which a British court will judge him will take into account the handicaps under which he works and the general standard of skill among his maritime colleagues. On the other hand, foreign courts can and do assume jurisdiction in actions for negligence committed on what to them is foreign territory, to wit, a British ship. In the event of a surgical mishap to a passenger from the United States a ship's surgeon might find himself the defendant in an action for negligence in the courts of California. The difficulty and inconvenience of defending himself in such an action need no stressing. If he allows judgment to go by default, or if he defends himself unsuccessfully in the Californian court so that judgment is entered against him, an action could be brought against him in the British courts on the Californian judgment; and, provided the California proceedings have been served on him, the ship's surgeon would almost certainly have no defense. Moreover, they "think big" in damage suits in California.

The shipping company cannot protect its surgeons from the consequences of an action for negligence, although it can protect itself from vicarious liability as employer by the terms of the tickets which it issues. But if an injured passenger sues the surgeon instead of or as well as the company, no condition on the ticket can exclude his liability, because the ship's surgeon is not a party to the contract between the passengers and the company of which the condition on the ticket is a term. The moral of all this is for the ship's surgeon to make sure that his medical insurance covers him outside of Great Britain.

BUSINESS PRACTICE

SPECULATION, GLAMOUR SHARES, AND SLEEPER STOCKS

Edward A. Merkle

The recent flood of warnings about the dangers of speculation makes it perhaps advisable to lay down a few ground rules to help the physician evaluate the spate of hot tips, hunches, and highly erratic glamour shares which currently deluge the financial community—and unfortunately are sometimes passed on to the public as "investment advice."

In a declining, or bear, market, warnings about speculation are generally unnecessary. Only the skilled professional investor, thoroughly informed amateur, or born gambler risks his money in the face of a widespread downward trend. But in an aggressive rising, or bull, market, speculation tempts almost everyone, and the average investor is not immune to the lure of fast capital gains.

Spearheading the recent breakthrough of the Dow Jones industrial averages of, first, the 600 level, and almost exactly two months later reaching the 630 point, has been a sustained though not al-

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President, Madison Fund, Inc.

ways justified interest in what is loosely called the space-age industries. These are comprised of groups of electronic, missile, aircraft, chemical-propellant, and similar companies which have active development programs and government contracts for various components which go into rockets and related guided projectiles.

Around the spectacular advances of these companies has developed an aura of glamour, an oft-expressed opinion even by professional investment advisors that every well-rounded portfolio must have a substantial holding in such stocks.

There is nothing new about this type of popularity bubble in the stock market. For at least 50 years there have been recurring rushes to participate in some highly promoted industry which appears momentarily to have unlimited possibilities. Those who witnessed, participated in, or suffered heavy losses in the Florida land boom of the 1920's will understand how this type of glamour is seeded, reseeds itself, blooms, and suddenly dies.

Currently, the glamour industries—which can be defined as those industries in which security prices have been inflated until they no longer have any relationship to forseeable earnings—are the group mentioned above. Already, individual companies in these fields have risen like balloons, and a few of them have descended just as precipitously as the same balloon when the gas escaped. A single government contract, substantial in itself but unlikely to repay development costs, let alone return a high profit, shoots a stock up 5 to 10 points in a single day's trading.

In this framework, it would be well to review historic parallels to today's glamour shares. In each case, both market advisors and much less sophisticated investors claimed that anyone not holding the then popular type of stock was bereft of his senses. A glance at a list of a half-dozen such instances—typical but by no means definitive—will be enlightening: (1) the Louisiana off-shore oil boom in 1957, when a leading stock rose to 76 only to decline to a low of 30 in 1959; (2) the post-war airline boom, when a typical issue sold at 20 in 1946, declined, and eventually, in 1955, returned to the same price; (3) the aircraft manufacturing ascension some years later, when one of the major manufacturers sold at 90 in 1954, a price which has not been reached in the interim, and is now at 60; (4) the drug stocks during the antibiotic boom, when a representative issue sold at 20 in 1951 and did not again exceed this figure until 1958; (5) the aluminum stocks, when the leading company sold stock at 136 in 1956 and at a low of 60 in 1958; and (6) the uranium stocks, when one company went from a high of 25 in 1955 to a low of 15 in 1958.

The companies referred to in these examples, it should be emphasized, are not exceptions or low-grade speculations. They are leading firms, with well-seasoned securities, several of which approach blue-chip quality over the long term. But they are also in cyclic industries, subject to inflationary pressures.

If, on the one hand, the investor should be sensitive to the dangers inherent in belated participation in glamour industries, he should also have a heightened awareness of the potential inherent in uncovering an undervalued situation among the blue chips of the future. These undervalued securities, or "sleeper stocks," are found among companies not generally well-known to the investing public, yet are usually sound aggressive organizations with the courage to spend large sums for research in new products or improvements of existing ones.

The changing economic scene is one of chief stimuli to the development of a bona fide sleeper. A soundly financed organization with accurate research into industrial trends will far outstrip its better-known, stand-pat competitors, and in the process will become both a profitable business and an excellent investment opportunity.

The basic criteria for an undervalued stock are (1) excellent quality as an investment, independent of potential because of their record of long-term earnings and return on invested capital; (2) sufficient volume of shares outstanding that even a large new holding will not create a scarcity value for the stock; (3) prospects of sharply improved earnings or increased stature, though not necessarily in the immediate future, through new products, new industries, or other specific areas; and (4) facilities, working capital, management skills, and other vital resources adequate to realize the potential.

For a large investment fund, the size criterion is frequently the main deterrent, forcing management either to take a special position amounting to partial control of the company or to relinquish the opportunity. But for the individual investor, with markedly smaller holdings, several sleeper stocks are essential in the well-diversified portfolio.

When the physician contemplates changing his portfolio, the recent bull market is both an opportunity and a challenge—an opportunity to upgrade his holdings and a challenge to his judgment, his investigative ability, and his resistance to over-optimistic forecasts. Almost without exception, investment fund managers have acquired new holdings or made important changes during the past six months. Nonetheless, the awareness that enthusiasm is contagious, and frequently unwise, is very immediate, and each individual transaction must be scrutinized with extreme care lest the technical correction which always follows a bull market result in severe asset reductions through improperly evaluated securities.

MEDICAL LITERATURE ABSTRACTS

INTERNAL MEDICINE

Effects of Periodic Mental Stress on Serum Cholesterol Levels. S. M. Grundy and A. C. Griffin. *Circulation* 19:496-498 (April) 1959 [New York].

The effects of quarterly final examinations on serum cholesterol levels in 2 groups of freshman medical students, between the ages of 20 and 31 years, were studied. During the 2 periods of examinations, at the end of the winter quarter and at the end of the spring quarter, the mean cholesterol levels were elevated significantly over those obtained during control periods of relative relaxation. The 2 groups, of 50 and 47 male students, showed respectively, a 16.5 and 11% increase in serum cholesterol levels during winter and spring quarter examinations. The exact relationship between elevated serum cholesterol levels and atherogenesis is not understood at the present time. The reported data suggest that emotional stress may be a factor that produces an increased cholesterol level in some persons and may influence the development of atherosclerosis. More extensive studies are needed to reveal the significance of these preliminary observations.

The Aortic Arch Syndrome (Pulseless Disease): A Report of 10 Cases with Three Autopsies. W. M. Thurlbeck and J. H. Currens. Circulation 19:499-510 (April) 1959 [New York].

The authors report on 5 men and 5 women, between the ages of 46 and 81 years, with absent or diminished arterial pulsations and blood pressure readings in one or both arms. Six of the 10 patients also had absent carotid arterial pulsations on one or both sides. The blood pressure was determined satisfactorily in 4 patients with the aid of a recording machine devised to record the Korotkov vibrations over the brachial artery when these are indistinct or inaudible on auscultation. The results obtained in these 4 patients indicated feeble arterial pulsations despite the inability to palpate them clinically. Seven of the 10 patients died, and autopsy was performed on 3. Severe atherosclerosis with superimposed thrombosis was revealed by microscopic examination. Two of the surviving patients received anticoagulant therapy with bishydroxycoumarin (Dicumarol) for periods up to 3 years. This resulted in subjective improvement and weak pulsations being palpable in the right radial artery in both patients and in the carotid arteries in one; these vessels had previously been clinically nonpulsatile.

A Symposium on Hodgkin's Disease: Based on a Series of 960 Cases Diagnosed Clinically. O. H. Warwick and A. H. Sellers. Canad. M. A. J. 80:423-429 (March 15) 1959 [Toronto].

The authors report on 960 patients whose condition was diagnosed clinically as Hodgkin's disease. The data were recorded on standard follow-up cards at 8 regional cancer treatment clinics of Ontario from 1932 through 1951. Of the 960 patients, the diagnosis was confirmed histologically in 730. Slides relating to 547 of the 730 cases were available for review, and of these 547 cases, 422 were "reconfirmed" as being Hodgkin's disease. Sixty-five cases were placed within the "malignant lymphoma" group, 12 were considered to be cases of malignant disease of other sites, 12 were considered nonmalignant, and 36 were not diagnosed. Of the remaining 422 patients whose cases were reconfirmed, only 23 were under 15 years of age, while 188 were under 35 years of age. About 4 out of 5 patients were treated by radiotherapy alone. Radiotherapy with chemotherapy, surgery with radiotherapy, surgery alone, and chemotherapy alone comprise the other forms of treatment, in that order. There was no significant difference in the 5-year survival rates for those patients diagnosed clinically as having Hodgkin's disease, those with a diagnosis confirmed histologically, and those reconfirmed as having Hodgkin's disease (crude survival rate was 30%; adjusted survival rate, 32%).

There are acute and chronic forms of Hodgkin's disease. In the very acute case with symptoms and signs of generalized disease, one is justified in giving a grave prognosis. The chronic form may smolder for years without seriously disturbing the patient's way of life. It seems fair to say that, whereas one-third of the patients with Hodgkin's disease die within a year of diagnosis, those who survive to the 5-year and especially the 10-year mark have an increasingly favorable prognosis. Five

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The place of publication of the periodicals appears in brackets preceding each abstract.

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cases illustrating especially long survival are reported in detail. The patients were 4 males, aged 3, 4, 24, and 33 years, and one female, aged 19 years at time of onset of the disease. The diagnosis of Hodgkin's disease in these patients was established between 1931 and 1934; it was confirmed histologically and was reconfirmed on review in the course of this study. All five patients are well today and have thus survived 26 and more years.

Rupture of Thoracic Aorta in Course of Pulmonary Tuberculosis. J. M. Escudero Villar and J. Neyra Ramírez. Tórax 7:258-261 (Sept.) 1958 (In Spanish) [Montevideo, Uruguay].

Rupture of the thoracic aorta in the course of pulmonary tuberculosis is a rare accident. Two cases of pseudoaneurysm of the ascending aorta from tuberculosis erosion of the artery in patients with severe forms of pulmonary tuberculosis have been previously reported in the literature. A roentgenologic diagnosis of the pseudoaneurysm was made during the life of the patients. Both patients died, one from rupture of a pseudoaneurysm; an autopsy showed that the pseudoaneurysm was a tuberculous erosion of the ascending aorta on a segment in which the artery was in close contact with a lobe of the tuberculous lung. The authors report the case of a 62-year-old man who was hospitalized after a clinical and roentgenologic diagnosis of bilateral miliary pulmonary tuberculosis. After being treated with cough remedies, streptomycin, and isoniazid, this patient improved greatly in the course of 2 months. Cough and fatigue disappeared, there was a gain in weight, and the roentgenograms showed improvement of the pulmonary lesions. Aortic pseudoaneurysm or cardiovascular lesions were never suspected or discovered in the roentgenograms of the thorax. The patient suddenly had a mild attack of coughing, followed by hemoptysis, and died within 5 minutes. An autopsy showed a large hemorrhage into the pleura of the left lung, the thoracic aorta being firmly attached to the lower lobe of that lung. A perforation, 2 cm. in diameter, caused by tuberculous erosion, occurred on a segment of the wall of the thoracic (or descending) aorta. Histological study of the thoracic aorta showed tuberculous, caseous, perforating, periaortic lesions.

Albuminuria (Proteinuria) in Renal Diseases: II. Preliminary Observations on the Clinical Course of Patients with Orthostatic Albuminuria. S. E. King. New York J. Med. 59:825-832 (March 1) 1959 [New York].

The author reports preliminary observations on 300 young men with proteinuria (albuminuria), who were examined in several Army hospitals between 1950 and 1954 and were followed up for an average period of 6 years. Of the 300 patients, the original pattern of proteinuria was of orthostatic type in 191, of constant type in 49, and of transient (negative) type in 60. The orthostatic type of proteinuria persisted in 105 of the 191 patients; it changed to a constant pattern type in 60 (32%). Constant proteinuria remained unchanged in 40 of the 49 patients with an original constant pattern of proteinuria. Orthostatic proteinuria was found in 27 and constant proteinuria in 9 of the 60 patients who originally had shown a negative pattern of previously recognized proteinuria. Persisting proteinuria thus was demonstrated in 241 of the 300 patients.

In about 33% of the patients with simple orthostatic proteinuria, laboratory and clinical evidences of a variety of renal diseases were observed on follow-up. These included chronic glomerulonephritis and ill-defined glomerulitis, chronic pyelonephritis, congenital renal anomalies, urologic disorders, and the renal components of various systemic disorders including diabetes mellitus, hypertension, and the collagen diseases. These findings discredit the common belief that orthostatic-type proteinuria is a specific benign disorder of youth, which disappears in later life and is without clinical significance. It is not implied that all patients with orthostatic proteinuria invariably suffer from devastating renal disease. On the contrary, overt renal disease usually discovered beforehand is excluded from this clinical definition, leaving a residue of early or chronic latent renal disorders.

These observations clearly indicate that latency does not guarantee regression. On the contrary, it appears that over a long period of time these common miscellaneous latent renal disorders may constitute an important source of chronic renal disease in later life. Early recognition of the specific diseases manifested by orthostatic-type proteinuria may suggest therapeutic approach and investigative studies not feasible in advanced renal disease. These latent conditions with an apparently innocent form of proteinuria present a clinical and public health challenge in early diagnosis and control of many forms of chronic renal disease.

Clinical Picture of Tricuspid Stenosis. H. Blömer and W. Rudolph. München. med. Wchnschr. 101:495-500 (March 20) 1959 (In German) [Munich, Germany].

Recent progress in cardiac surgery makes the more exact identification of heart lesions of greater importance, and so the authors review the clinical aspects of stenosis of the tricuspid valve, a lesion which is often overlooked. Aside from rare exceptions, stenosis of the tricuspid valve is of rheumatic origin and is always combined with other valvular lesions, particularly mitral stenosis and aortic stenosis. Autopsy studies have revealed that it accounts for about 30% of rheumatic valvular lesions and that it is a sign of a particularly grave rheumatic heart disease, which is not limited to one valve. The authors list the following signs as important for the diagnosis of stenosis of the tricuspid valve: 1. A high and pointed presystolic wave is observed in the venous and liver pulse. 2. A presystolic and diastolic murmur is observed in the region of the tricuspid valve, which increases in volume during inspiration. Sometimes a tricuspid opening murmur can be heard in this region, and it also increases during inspiration. 3. In advanced cases of tricuspid stenosis there exists a general venous congestion with enlargement of liver and spleen and with ascites and edema. 4. The color of the skin is a muddy gray. 5. Roentgenography reveals extreme dilatation of the right atrium with no evidence of enlargement of the right ventricle and of the pulmonary artery and without signs of pulmonary congestion. 6. The electrocardiogram shows a high and pointed P wave as evidence of atrial hypertrophy without signs of hypertrophy of the right ventricle. The occurrence of atrial fibrillation makes the diagnosis more difficult since many of the typical symptoms disappear.

As regards the prognosis of tricuspid stenosis, the authors say that it is unfavorable in young persons, because it signifies florid rheumatic heart disease. In patients of more advanced age, however, tricuspid stenosis exerts a favorable effect on the hemodynamic results of mitral and aortic stenosis and may thus actually prolong the life of these patients. While in recent years attempts have been made to treat tricuspid stenosis surgically, the authors emphasize that, in view of the hemodynamic effects of tricuspid stenosis in older patients, tricuspid commissurotomy should never be carried out without the simultaneous opening of the mitral stenosis, because, by removing the protective mechanism for the pulmonary circulation, there is danger of acute pulmonary edema.

Some Statistical Investigations in Diabetes Mellitus. B. Vinke, W. F. Nagelsmit and F. S. P. van Buchem. Diabetes 8:100-104 (March-April) 1959 [New York].

The authors report on 733 male and 1,379 female patients with diabetes mellitus who were treated at the clinic for internal diseases of the State University in Groningen, The Netherlands. Women predominated, particularly among the patients 50 years of age or older. There was no correlation between the incidence of diabetes in women and the number of children born of them; the chance of acquiring diabetes does not appear, therefore, to be greater with increasing parity. "Diabète maigre," a form of diabetes mellitus associated with low body weight, was observed in both young patients and patients of more advanced age, and "diabète gras," a form of diabetes associated with obesity, occurred particularly in adults over 30 years of age. The incidence of "diabète gras" was much higher among women (57%) than among men (22%). Findings in women indicated that obesity is a stimulating factor in the pathogenesis of diabetes mellitus and that the high incidence of diabetes in women over 50 years of age is associated with obesity. The unfavorable influence of obesity on diabetes mellitus was indicated by the higher insulin requirements among women with overweight and inadequate loss of weight as a result of the treatment.

Observations on the Pancreatic Islet Tissue of Young Diabetic Subjects. N. Maclean and R. F. Ogilvie. Diabetes 8:83-91 (March-April) 1959 [New York].

The authors examined pancreatic sections of 41 patients with diabetes mellitus, whose ages at the time of death varied between 11 months and 29 years. The pancreases of 22 nondiabetic patients who died at similar ages were used for comparison. Eighteen of the 41 diabetic patients had died within 8 weeks of the onset of symptoms, i. e., in the acute stage of the disease, and 23 had died at intervals ranging from 9 months to 19 years after the onset of diabetes mellitus, i. e., in the chronic stage of the disease. The size of the islets of Langerhans and the proportion and weight of islet tissue were greater in the specimens obtained from patients with acute diabetes than in those obtained from patients with chronic diabetes. In both groups these values tended to decline with increasing duration of the disease; this decline was rapid in patients with acute disease, and it was slow in patients with chronic disease. In patients with acute diabetes the islets were larger than in the nondiabetic patients, and in some of them the proportion and weight of islet tissue were normal.

The pattern which appears to emerge from these observations is that diabetes mellitus in young persons may be accompanied by initial hyperplasia of the islets, may occur in some patients who have a normal quantity of pancreatic islet tissue, and may result within a few weeks in diminution of islet tissue to levels which are usually met with in young patients with chronic diabetes; thereafter there is a gradual decline in the proportion and weight of the islet tissue. In both groups of young diabetic patients studied, the pancreatic findings were not inconsistent with Young's concept of the causation of diabetes mellitus in man. They also suggested that young diabetic patients, dying in coma shortly after the onset of the disease, resemble in some respects elderly obese patients with diabetes. Both may exhibit insulin resistance and may possess large islets and relatively normal quantities of islet tissue. These similarities are of some interest, since Young attributes the clinical differences and end-results of diabetes mellitus in the young and old to differences in intensity and duration of pituitary stimulation. The authors' observations merely suggest that a metabolic disorder which causes initial hyperplasia of the pancreatic islets and later degeneration of the beta cells may exist, and that it may be a factor in the causation of diabetes even in patients with normal amounts of islet tissue.

Laboratory Acquired Tularemia in Vaccinated Individuals: A Report of 62 Cases. T. E. Van Metre Jr. and P. J. Kadull. Ann. Int. Med. 50:621-632 (March) 1959 [Lancaster, Pa.].

From 1944 to 1956 laboratory-acquired tularemia was observed at Fort Detrick, Frederick, Md., in 62 persons who had received one or more courses of a phenolized and/or acetone-extracted tularemia vaccine. Cases were detected by screening of personnel who experienced contact with Pasteurella tularensis during their work. The development of illness in one of these individuals or the occurrence of a break in technique resulting in possible exposure to Past. tularensis inaugurated clinical and laboratory investigations for evidence of tularemia. The 62 cases of laboratory-acquired tularemia in vaccinated persons included those of 9 patients with ulceroglandular disease. Six patients incurred minor injuries by objects contaminated with tularemia bacilli—a hypodermic needle in 2 instances, an autopsy tool in 1, and broken glass in 3. The lesion appeared at the site of trauma usually after 1 to 3 days. Initial papuloerythematous lesions developed on a finger or hand in all the patients but progressed to ulceration in only 3 cases. Regional lymph nodes were enlarged and tender. Constitutional reactions were absent in 4 patients, but they were characterized by malaise, chilliness, and oral temperatures of 101 to 102 F (38.3 to 38.8 C) in 2 and by severe prostration and temperatures exceeding 103 F (39.4 C) in 3. Past. tularensis was isolated from local lesions in 6 cases. Seven patients received systemic antibiotic therapy, consisting of streptomycin in 3 cases, chlortetracycline in 1, and a combination of streptomycin and chlortetracycline in 3. Response to each regimen was satisfactory.

Forty-three patients had typhoidal tularemia. Thirty-eight of these patients were working with the organism; 9 of them sustained exposure to uncovered or spilled cultures, with illness appearing after 2 days in 1, 3 to 5 days in 6, and 7 days in 2. Five patients had not worked with the organism but had entered the tularemia laboratories. All patients had fever and malaise. Thirty-three had localizing symptoms and signs suggesting respiratory tract infection. Chest x-rays were obtained in 34 cases and revealed evidence of bronchopneumonia in 11. Antitularemia agglutinin titers rose to 1:1280 or above in all 43 patients. Twenty-eight of the 43 patients received specific antibiotic therapy within the first 30 days of illness. A variety of drugs were used, alone and in combination, including bactericidal agents, such as streptomycin and dihydrostreptomycin, and bacteriostatic agents, such as the tetracyclines and chloramphenicol. No chronic disability developed in any patient treated with these agents for 3 or more days within 30 days of onset of illness. Fifteen patients received no specific antibiotic therapy during the first 30 days of illness; 11 were observed before effective drugs were available. Five individuals had symptoms for 5 months or longer, despite a late course of antibiotics in 4 instances. Seven patients recovered spontaneously within one month, and 3 responded promptly when specific antibiotic therapy was finally administered. Chronic disability was more frequent in this group than in those treated during the first month of the disease.

There were 10 cases of asymptomatic tularemia. Six persons were working with the organism, and none of these recognized an overt exposure; 4 had not worked with the organism but had entered the laboratories. The diagnosis was established in retrospect on the basis of one or more serum agglutinin titers of at least 1:1280 observed 8 or more months after the last immunization. The authors conclude that the efficacy of the vaccine cannot be evaluated completely.

Budd-Chiari's Syndrome Diagnosed by Means of Phlebography in a Case of a Retroperitoneal Sarcoma. M. Levander and J. Pontén. Acta med. scandinav. 163:251-255 (no. 3) 1959 (In English) [Stockholm].

The authors report on a 57-year-old woman with the Budd-Chiari syndrome, consisting of an occlusion of the hepatic veins followed by stasis and swelling of the liver, ascites, and abdominal pain. The spread of the occlusive process upwards into the vena cava and even into the right heart complicated the clinical aspect by causing dyspnea of an unusual character, which diminished on the patient's lying down. It also caused difficulties in the differential diagnosis from a constrictive pericarditis. Roentgenography of the inferior vena cava revealed a definite obstruction to the passage of the catheter at the level of the diaphragm; below the obstruction there was an 8-cm.-long segment of partial obstruction of the inferior vena cava. A rich anastomotic net was visible around the vertebral column. The right anterior aspect of the inferior vena cava was somewhat angled in its course at the level of the hilus of the liver, signifying a deformation by an expansive process. These observations made it possible to arrive at a correct diagnosis.

The patient was treated with diuretics and anticoagulants (bishydroxycoumarin and heparin). About 2 weeks after the roentgenography of the inferior vena cava, the patient complained of a sudden severe headache. Despite the absence of neurological signs and rigidity of the neck, a cerebral hemorrhage seemed to be the cause. The heparin treatment was discontinued, but the patient died. Autopsy revealed a retroperitoneal sarcoma which had grown into the lumen of the inferior vena cava and almost completely occluded it. The tumor also filled a considerable part of the right auricle and bulged downwards into the orifice of the tricuspid valve, which explained why the patient had an unusual type of dyspnea which diminished in the recumbent position. There was a massive fresh subdural hemorrhage, the cause of which was not found.

The Budd-Chiari syndrome gives rise to a characteristic picture of posthepatic portal hypertension. The spread of the occlusive process upwards into the vena cava may cause difficulties in the differential diagnosis, and in many cases it may not be possible to arrive at an exact diagnosis without catherization of the liver, with pressure measurements complemented by injections of a contrast medium. A biopsy of the liver can be of great value in estimating the character of the changes in the liver. With anticoagulant therapy commenced early, the prognosis in cases of thrombosis of the hepatic veins ought to improve considerably.

Clinical and Virologic Studies on Acute Epidemic Exanthem (So-Called "Blister Disease"): 1. Discussion of Cases and of Attempted Isolation of Etiologic Agent. G. Enders-Ruckle, H. J. Heite and R. Siegert. München. med. Wchnschr. 101:490-494 (March 20) 1959 (In German) [Munich, Germany].

During the second half of 1958 an exanthematous disease assumed epidemic proportions in Germany. It was first observed in northern Germany and then spread to the south and the west. In newspaper reports the disease was referred to as "blister disease." The first medical reports called attention to its symptomatologic similarity to erythema infectiosum, but now after longer observation opinions are divided in that some accept its identity with erythema infectiosum and others reject it. Erythema infectiosum, which is generally accepted as a disease of childhood and is often referred to as "fifth disease," varies greatly in the morphology of the skin eruption, so that it has also been designated as "erythema variabile." This great variability doubtless is a cause of the nosological problem presented by the so-called blister disease.

The authors feel that only investigations into the etiology will solve the question. They present the clinical histories of 14 patients with blister disease in whom attempts were made to isolate an etiological agent. Studies were made on 10 throat irrigation fluids, obtained during the first 5 days after the eruption of the exanthem, and on 19 stool specimens obtained between the 1st and the 14th day. Other materials available for study were: One heparinized blood specimen from the 4th day of the disease; one cerebrospinal fluid specimen from the 2nd day; one skin biopsy specimen from the 4th day; the fluid content of a large skin blister from the 6th day; and from all patients 1 to 3 blood specimens for serologic studies. Twelve cytopathogenic agents were isolated from throat washings and stool specimens with the aid of culture in monkey-kidney tissue and in human tissue. Six of these, which were examined for their cytopathogenic behavior and for their tissue affinity in cell cultures, exhibited far-reaching conformity. Further attempts at identification, which are to be described in a later report, indicated that there was no complete serologic conformity, but that there are 2 types with relations to the ECHO group as well as the Coxsackie group of viruses.

Effects of Repeated Poisonous Snakebites in Man. H. M. Parrish and C. B. Pollard. Am. J. M. Sc. 237:277-286 (March) 1959 [Philadelphia].

Three concepts are commonly held regarding the effects of repeated poisonous snake bites in the same person: 1. Repeated envenomations will render the victim immune to venom and lessen the danger of future bites. 2. The individual will develop an allergy to the complex proteins of the venoms, making each subsequent bite more dangerous and inviting the possibility of an anaphylactic reaction. 3. Previous poisonous snake bites will have no effect on subsequent bites. The patients whose case histories are analyzed in this study were all professional herpetologists, snake handlers, wild animal dealers, or biologists. All were adult males, ranging from 22 to 45 years of age, who at the time of interview were apparently in good health. Of the 14 men, 1 had experienced 12 poisonous snake bites; 1, 10 such bites; 2, 6 bites; 1, 5 bites; 3, 4 bites; 1, 3 bites; and 5, 2 bites. Thus, these 14 men had experienced a total of 64 poisonous snake bites. The anatomic sites of these bites were as follows: 36 on the fingers or thumb, 10 on the forearm, 8 on the hand, 7 on the leg, and 3 on the foot. All but 3 of the snakes inflicting these bites were North American pit vipers.

Five patients had permanent local defects as a result of snake bites. One patient had his thumb amputated, and 3 others had atrophy, limitation of motion, and a permanent deformity of a digit; these defects resulted from necrosis, gangrene, and infection after envenomation. The 5th patient had atrophy of the shoulder muscles resulting from a poisonous snake bite on the forearm of the involved side; the muscle atrophy probably resulted from a neuritis associated with serum sickness following antivenin (horse serum) therapy. There was no clinical or laboratory evidence that these patients developed permanent immunity to pit viper venoms. The lack of permanent immunity was attributed primarily to the prolonged and irregular intervals between envenomations and the short latent period between a bite and the development of clinical envenomation which does not allow sufficient time for a "booster effect" on antibody production. Other possible contributing factors were bites by different species of snakes, antivenin inhibition of active immunity, and inconsistencies in the doses of venom injected.

Thirteen of the 14 patients with repeated envenomations were scratch-tested for snake venom allergy. Of these, 4 were found allergic to rattlesnake or moccasin venoms, or both. Some patients exhibited allergy to the venom of snakes zoologically related to the species which bit them. For example, a patient may become allergic to moccasin venom even though he was bitten previously by rattlesnakes. The severity of the effects of repeated snake bites in nonallergic patients depends on the characteristics of the individual envenomation and not on the cumulative effects of previous snake bites.

The Diagnosis of Tularaemia, with Particular Reference to Difficulties Presented by Atypical, Abortive and Asymptomatic Forms of the Disease. O. Ljung. Acta med. scandinav. 163:243-249 (no. 3) 1959 (In English [Stockholm].

The authors performed Pasteurella tularensis agglutination and intradermal tests on 3 men and 3 women, between the ages of 37 and 63 years, who for clinical reasons were suspected of having tularemia. With the aid of these tests, a diagnosis of ulceroglandular tularemia was made in 4 of the 6 patients; a diagnosis of tularemia resembling the ulceroglandular type of this disease, despite the absence of ulcers and enlargement of lymph nodes, was made in 1 patient; and a diagnosis of cancer of the thyroid with metastases was made in the last patient. In patients who for clinical reasons are suspected of having tularemia, a positive reaction to the intradermal or the agglutination test suggests a diagnosis of tularemia. The diagnosis of acute tularemia is rendered difficult by the fact that only a few patients present the typical manifest form of the disease. Most forms of tularemia are atypical, abortive, and asymptomatic. Patients, with these common and less conspicuous forms of the disease, just as those with the typical forms, have positive results from the agglutination and intradermal tests, both of which—and the latter in particular—may be obtained over a period of many years. It should be emphasized that, since a high agglutination titer and a strongly positive reaction to the intradermal test may continue for a long period, both of these responses indicate only that the infection has taken place and do not prove that the current disease is tularemia. A negative reaction to the agglutination test in the first week and rising titers in the following weeks provide the most reliable support for a diagnosis of acute tularemia.

A moderately increased agglutination titer in the first week, which does not show further increase in the weeks immediately following, would seem to contradict a diagnosis of acute tularemia and would suggest rather that these moderately increased titers are the result of an earlier infection. The agglutination test is a rough and erratic diagnostic method. Variations of up to 4 times the value of the titer for simultaneously drawn specimens are not uncommon, and for this reason in doubtful cases an unfortunate combination of, for instance, 2 tests may tend to support an erroneous diagnosis. The patient with cancer of the thyroid came from a district with high incidence of tularemia, but there was no history of past tularemia. The patient showed a typical positive reaction to the intradermal test, which revealed that infection had occurred. Of 2 simultaneously drawn agglutination specimens, one yielded a negative result and the other a positive result, with a titer as low as 1:10. The agglutination titer after one month was 1:160 in one specimen and negative in the other. Two days later titers of 1:80 and 1:40 were observed. If acute tularemia would have been suspected in this patient with cancer of the thyroid, the 2 first tests would have confirmed the diagnosis, whereas the second tests would have contradicted it.

SURGERY

Some Observations on the Cause and Treatment of Hare-Lip and Cleft Palate, Based on the Treatment of 1041 Patients. M. C. Odfield. Brit. J. Surg. 46:311-321 (Jan.) 1959 [Bristol, England].

The author operated on 1,041 children, 596 boys and 445 girls, with harelip, harelip and cleft palate, or cleft palate alone. Of the 233 patients with harelip, 94 (40%) were girls and 139 (60%) were boys; of the 450 patients with harelip and cleft palate, 137 (30%) were girls and 313 (70%) were boys; of the 358 patients with cleft palate alone, 214 (60%) were girls and 144 (40%) were boys. Other congenital abnormalities were associated with the harelip or cleft palate in 92 of the 1,041 patients. The cause of harelip and cleft palate is not known, but 2 factors of proved significance have emerged, i. e., inheritance and unfavorable maternal environment during the "critical period" of the 12 first weeks of gestation until the palate of the embryo has fused.

The methods of surgical treatment and the results obtained are described. Of 397 patients who have been reviewed for speech results, 303 (77%) obtained excellent results, 71 (17%) obtained fair results, and 23 (6%) obtained poor results. Of 494 patients reviewed after the operation for repair of the palate, favorable results were obtained in 467

(94.4%) and poor results in 27 (5.6%). The lip should be repaired only when the infant is thriving and after attaining the weight of about 12 lb. (5.4 kg.). The Le Mesurier rectangular flap method was used for a complete unilateral harelip with severe nostril deformity, but a simple straight excision technique (Kilner) was used for minor unilateral and bilateral harelip cases. Satisfactory results can be obtained by the well-tried method of Wardill and Kilner for repair of the palate. The posterior palatine arteries should never be divided. The nasal mucosa above the hard and soft palates should be closed by absorbable (catgut) sutures, as well as the muscles of the soft palate and buccal mucosa. It is more important to provide a strong arching soft palate than a long flaccid one. Length is not as important as muscularity and mobility. Operations involving incisions in the posterior pharyngeal wall and muscle transplants should be avoided in all primary cases. The ideal age for repair of the palate is between 1½ and 2 years.

Structural Alterations of the Myocardium Resulting from Massage of the Heart: Immediate and Late Histological Observations. F. Caluzzi, E. Perazzo and F. Margaglia. Minerva chir. 14:31-35 (Jan. 15) 1959 (In Italian) [Turin, Italy].

The immediate and late histological alterations of the myocardium and the epicardium, resulting from hand massage of the heart, were studied in 39 dogs that had been subjected to thoracic surgery. To relieve cardiac arrest which had occurred in all the animals, hand massage was performed at once, and adequate doses of stimulants to induce contraction of the myocardium were eventually given. Twenty-two animals failed to respond to the treatment. The heart beat was reinstated in 12 animals, but they died of severe cardiovascular collapse within 18 hours after the operation. Two of the surviving 5 animals died in intervening complications not related to the cardiac arrest one month after the operation; the remaining animals were killed 35 to 47 days after the operation.

A histological study was made of large sections of the myocardium stained with hematoxylin and eosin or with Van Gieson's stain. At macroscopic examination, diffused hemorrhagic effusions, with focal distribution in the subpericardium and in the deeper layers of the ventricular wall, were observed in the dogs that died during massage of the heart. The muscular fibers showed no substantial alterations. Rupture of the heart during the massage occurred in one animal only. The rupture extended to the most superficial layers of the heart; it was a 2-cm.-long longitudinal rupture, parallel to the direction of the muscular fibers, and it let out small amounts of blood. Effusions into the epicardium were found mostly in the ventricles, which were the part of the heart that came in most direct contact with the hand. Lesions were also present in parts of the heart, such as the atrial walls, which were not subjected to pressure of the fingers. On opening the heart, hemorrhagic infiltrations were also found in the endocardium. Traumatic lesions of the tendinous cords were present in some animals. Microscopic examination showed bloody infiltrations which, though not extensive, were so marked in some cases that they separated the muscle fibers. The epicardium was damaged more than the endocardium. Slightly different findings resulted from examination of the hearts of animals that died some hours after massage of the heart had been performed. Accumulation of large mononuclear cells, lymphocytes, and plasma cells was observed in some of these animals.

Late observations made on the dogs that died one month after massage of the heart or that were killed revealed some alterations in 3 dogs. Two of these dogs, however, had died of pyopneumothorax, and the authors believe that the alterations could have been the result of inflammation caused by this condition. Pericardial alterations consisting of limited but strong fibrous adhesions which linked the pericardium to the epicardium were found in the third animal. The massage caused no alterations in the endocardium or the pericardium of the remaining animals. The authors believe that the immediate alterations caused by hand massage of the heart are reversible, especially if they are not too severe or too extensive, even in cases of intervening inflammation.

Relapses After Surgery for Pulmonary Tuberculosis: A Study of 527 Cases After Resection and Collapse Therapy. O. Peräsalo, H. Heikkilä and T. L. Jalas. Ann. chir. et gynaec. Fenniae 48:1-18 (no. 1) 1959 (In English) [Helsinki].

The authors compared the postoperative relapses and the results of collapse and resection therapy in 527 patients treated at the Helsinki Tuberculosis Sanatorium from 1949 to 1957. The ages of the patients ranged from 17 to 57 years; the majority were between the ages of 21 and 40 years. Thoracoplasty had been performed on 276 patients; extrapleural pneumolysis, on 98; and partial pulmonary resection, on 153. The duration of preoperative hospital treatment varied from a few weeks to 3 or 4 months. The follow-up period varied in the cases of thoracoplasty and pneumolysis from 1½ to 8 years and in those of resection from 6 months to 7 years. At the end of the observation period the number of primary and secondary cures among the 276 patients subjected to thoracoplasty was 193 (71.29%), and the number of patients who were still ill was 44 (15.9%). The immediate mortality rate was 2.5%. Late tuberculous complications proved fatal in 8.6%. Three patients were lost to follow-up. The number of primary and secondary cures among the 98 patients subjected to pneumolysis was 81 (84.4%), and the number of patients who were still ill was 12 (12.5%). The immediate mortality rate was 2.1%. One patient died 4 years after the operation as the result of tuberculous complications. Two patients were lost to follow-up. The number of primary and secondary cures among the 153 patients subjected to pulmonary resection was 138 (90.2%), and the number of patients who were still ill was 5 (3.3%). Six patients died during the operation, and 4 died of late tuberculous complications. Five patients were lost to follow-up.

The patient's age and sex, earlier relapses, nature of tuberculous process, and preoperative sputum probably played a part in the development of relapses. Patients under 20 years of age, who underwent thoracoplasty or pneumolysis, demonstrated a high relapse rate. In the age range of 21 to 30 years, the relapse rate among those who underwent thoracoplasty or pneumolysis was lower, but then the relapse rate increased and reached a maximum among those in the age range of 51 to 60 years. Such differences between age groups were not observed among the patients who underwent pulmonary resection. The occurrence of relapses in the different operation groups was likewise compared. Resection proved clearly more favorable than the others, the relapse rate among those who underwent this operation being 9.8% as against 33.0% among those who were subjected to thoracoplasty and 21.4% among those who underwent pneumolysis. In all age groups the relapse rate was higher among men than among women. The relapse rate among patients who underwent resection for the first time was lower than among those who had had one or more relapses previously. A markedly high relapse rate of 55.3% was noted among patients with extensive cavitational changes who had undergone thoracoplasty or pneumolysis, whereas it was 12.9% among those who had undergone resection. Data show clearly that the number of relapses among patients with sputum positive for Mycobacterium tuberculosis was markedly higher than among those with sputum negative for Myco. tuberculosis.

A comparison of the follow-up results in patients subjected to collapse therapy, notably thoracoplasty, and the corresponding results obtained by pulmonary resection showed that the latter were more favorable. However, allowance must be made for differences in preoperative and postoperative treatment in the 2 therapies. The patients who underwent resection had invariably received preoperative and postoperative medication for a longer period than those who underwent thoracoplasty; prolonged treatment in most cases resulted in rendering the process quiescent. It is emphasized that both preoperative and postoperative medication should receive particular attention owing to the nature of tuberculosis. With long and uninterrupted preoperative treatment the process must be rendered as inactive as possible, and, on the other hand, it seems that the chance of relapse can be minimized by sufficiently long postoperative medication.

Experiences with Direct-Vision Repair of Congenital Cardiovascular Disorders Using the Rotating Disc Oxygenator. P. W. Sanger, F. H. Taylor, F. Robiscek and others. North Carolina M. J. 20:89-95 (March) 1959 [Winston-Salem].

The authors performed open cardiotomy with the use of the rotating disk oxygenator on 28 patients, between the ages of 1 and 17 years, with congenital heart disease. The principle of this oxygenator consists of gravity drainage of all venous blood into a reservoir; from there it is passed into an oxygenating cylinder in which many thin stainless-steel disks are rotating. The films of blood picked up by these rotating disks pass through an atmosphere of oxygen and back into the cylinder pool. From here the oxygenated blood is pumped into the arterial system of the patient. With the exception of 4 patients with pure valvular pulmonary stenosis, the operations on all the patients were performed in elective cardiac arrest. The time of cardiotomy varied from 3 to 41 minutes, with an average of 18 minutes. The time of perfusion ranged from 6 to 58 minutes, with an average of 26 minutes. The preoperative diagnosis of the various congenital defects proved to be correct at operation in every case.

There were 3 operative deaths. In the first patient an attempt was made to close a large common ostium connecting all 4 chambers of the heart by using the remainder of the atrial septum, but the suture line occluded the left atrial outflow. This error was corrected by reopening the defect, but the heart reacted very poorly, and the patient died within 3 hours after the operation. The second patient was operated on for tetralogy of Fallot, but very severe bleeding prevented repair of the interventricular communication, and death resulted within 6 hours after the incomplete repair. The third patient, with a large interatrial communication and a moderate displacement of the tricuspid valve, died of cerebral thrombosis on the third postoperative day. These 3 deaths represent an over-all operative mortality of 10.7%. Complete surgical repair of the congenital cardiac defect was performed on all the survivors, and each of these 25 patients is doing well.

The rotating disk oxygenator is a simple and safe machine. None of the operative losses was directly due to its use. The authors believe that, by using accurate methods of diagnosis, precision in performing the cardiopulmonary bypass, and adequate postoperative care, the feared complications of extracorporeal circulation, such as heart block, acute heart failure, fatal bleeding, air and fibrin emboli, may be avoided.

Fatal Pulmonary Embolism: A Ten-Year Study. S. J. Goldowsky and W. I. Carney. Am. J. Surg. 97:274-278 (March) 1959 [New York].

The diagnosis of pulmonary embolus in a living patient is subject to error, or may be missed entirely. The clinical diagnosis of peripheral venous thrombosis is certainly unreliable. In patients who have died and have been examined post mortem, at least the diagnosis is correct, and so the authors based their study primarily on autopsy material. They reviewed fatal and nonfatal emboli, verified at autopsy, at the Rhode Island Hospital in Providence during the 10 years from 1947 to 1956 inclusive. They found 58 cases of fatal pulmonary embolus, and in 206 additional cases pulmonary embolus was either a contributing cause or an incidental finding. Since a total of 3,683 autopsies were performed during this period, the incidence of fatal embolism in patients undergoing autopsy was 1.6%. The over-all autopsy rate for the hospital was 42.3%. Projecting these figures to the total number of deaths gives 137 fatal emboli and 487 nonfatal emboli in terminal cases, or a total of 624. During this same period the cross files of the medical record library show a total of 425 fatal and nonfatal emboli. Since the aforementioned projected figure does not take account of emboli in patients who survived, the latter number obviously represents a gross underestimate of the true incidence. This bears out the view that clinical diagnosis of pulmonary embolism is unreliable for statistical purposes. If the cases of pulmonary embolus are tabulated by year, there is no clear-cut evidence that their incidence has been altered by prophylactic or therapeutic measures now available.

The group of 58 patients having verified fatal emboli included 32 women and 26 men. The average age of the patients was 67.8 years; 42 were between 50 and 79, and 19 were between 70 and 79. Forty of the 58 fatal embolisms involved medical and 18 involved surgical cases. These figures corroborate previous reports of increased incidence with advancing age, and greater prevalence in medical disease than in surgical or postoperative states. A further breakdown of the 40 medical cases revealed that 19 of these patients had some form of active heart disease (e. g., failure, infarction, or rheumatic disease with fibrillation), while 10 harbored a malignant neoplasm. In the group of 18 surgical cases, there was an even division between general surgery and the surgical specialties. The relatively high incidence following hip nailing for fractured femur should be emphasized. The time interval between surgery and death from embolism ranged from 2 to 38 days; most of the deaths occurred between the 5th and 16th days. Only 2 of the 58 patients who died of embolism had had prophylactic vein ligations. One of these patients, who had been hospitalized with a diagnosis of pulmonary infarction, was subjected to bilateral superficial femoral vein ligation in continuity without exploration for thrombus, and was then placed on anticoagulant therapy. On this regimen he succumbed to a fatal embolism. The other patient died of an embolus after thigh amputation and homolateral vein ligation in continuity. Four patients died despite what appeared to be adequate anticoagulant therapy. One surgical patient is known to have undergone bandaging of the legs.

The incidence of fatal pulmonary embolus remains high despite an active interest in its prevention. Since it occurs mostly in elderly patients, any progress in its control could be obscured by the increasing age of the hospital population. The authors do not suggest that currently popular methods of prophylaxis or treatment are useless or should be discarded. It is quite posible that a number of lives have been saved by them. The available methods should be used, but their limitations should be recognized. Vena cava ligation and ovarian vein ligation may occasionally be lifesaving measures. Once an embolus has occurred, both vein interruption and anticoagulants should be used.

The Surgical Approach to Ulcerative Colitis. M. M. Ravitch. Wisconsin M. J. 58:147-151 (March) 1959 [Madison].

The author performed one-stage pancolectomy (total colectomy and abdominoperineal resection of the rectum) on 20 patients with ulcerative colitis at the Johns Hopkins Hospital in Baltimore and at the Mount Sinai Hospital in New York. In 4 of the 20 patients anal ileostomy was added to the pancolectomy. One woman, profoundly ill with ulcerative colitis, who had had a Noble plication procedure of the ileum added to her pancolectomy, died, the only patient in this series. She tolerated the operation very well, but the ileostomy failed to discharge, and exploration revealed obstruction to the plicated intestine. As the intestine was being released, a so-called cardiac arrest occurred in the patient whose condition had been good. From this she was resuscitated, but ultimately died after some days of decerebrate life. Pancolectomy is the preferred procedure for patients requiring operation for ulcerative colitis. The less profoundly ill patients will tolerate the one-stage procedure without difficulty and will be spared the risk of additional anesthesia, incision, and operative procedure. The more profoundly ill patients will derive sufficient benefit from the ablation of the diseased intestine to compensate for the moderate increase in magnitude of the operative procedure and will be spared the dangers of sepsis or hemorrhage attendant on retention of the diseased rectum in ulcerative colitis. Such patients can tolerate the operation more readily than they can the retention of the diseased intestine.

Criotherapy of Pigmented Spots in Children. N. I. Kondrashin. Khirurgiya 35:91-93 (no. 2) 1959 (In Russian) [Moscow].

The author recommends criotherapy (freezing with carbon dioxide snow) for the treatment of pigmented nevi of the face. Surgical treatment should be resorted to only when pigmented nevi are located on parts of the body hidden by clothes. Carbon dioxide snow is applied for 25 to 50 seconds. The treatment is repeated 14 to 21 days after the disappearance of the inflammatory reaction at the site of the pigmented stain. Gradually the spot becomes paler; the hairs fall out and do not regrow. A not very distinct depigmented spot remaining after the treatment gradually disappears. The average duration of treatment (5 to 10 criotherapeutic applications) depends on the size of the spot. Treatment of pigmented nevi may be carried out even in a 2-week-old infant. This treatment was used in 75 children under 14 years of age during the period from 1952 to 1956. Fifty children were followed up for 3 years. The nevus disappeared entirely in 16 patients; a mild depigmentation of the skin remained in 28; and in 6 pronounced loss of pigment, atrophy, or scars were present. Criotherapy is devoid of serious complications and is an effective treatment of congenital pigmented nevi of children.

Peripheral Vascular Grafts: Experimental Comparison of Autogenous Veins, Homologous Arteries, and Synthetic Tubes. W. A. Dale and G. E. Mavor. Brit. J. Surg. 46:305-310 (Jan.) 1959 [Bristol, England].

The authors report experiments carried out on 153 dogs which were subjected to peripheral shunt arterial grafting at the surgical experimental laboratory of the University of Rochester Medical Center in Rochester, N. Y. Grafting was performed with 43 homologous arteries obtained from dogs killed in the laboratory for other purposes, with 42 autogenous veins obtained from the dogs on which grafting was done, and with 68 synthetic tubes. Comparison of the results obtained showed that in terms of patency both autogenous veins and homologous arteries were superior to various synthetic tubes. The over-all patency rate for autogenous veins was 64%, for homologous arteries 77%, and for the total of the various synthetic tubes 29%. The reason for poorer results with the synthetic tubes, as compared with arteries and veins, appears to lie in the thickness of the pseudointima which occasionally lines the inside of the synthetic tube and which does not occur in either the autogenous vein or the homologous artery. Peripheral vascular grafting experiments in the dog, therefore, are considerably more critical for differentiating between grafting materials than is aortic replacement. While dilatation and formation of aneurysm are known to occur relatively frequently when a large vessel, such as the aorta, is replaced by an autogenous vein, this is unlikely when the vein replaces a smaller peripheral artery because of the lower tension on the wall of the replacing vein.

Clinical practice in the University of Rochester Medical Center has been strongly influenced by the reported laboratory results of experimental peripheral vascular grafting. Clinical policy was changed from the previous use of homologous arteries to the present use of autogenous veins for peripheral shunt replacement of atherosclerotic lesions of the femoropopliteal system. Early results in 28 patients have been satisfactory.

Surgery in the Treatment of Low-Back Pain and Sciatica: A Follow-up Study. F. C. Reynolds, A. E. McGinnis and H. C. Morgan. J. Bone & Joint Surg. 41A:223-235 (March) 1959 [Boston].

Of 205 patients who were operated on for intervertebral disk lesions between 1946 and 1952, only 115 (70 men and 45 women) returned for follow-up examination. There were 145 operative procedures carried out on the 115 patients; 134 of the surgical interventions were associated with removal of disk tissue. The average stay in the hospital was 11.6 days. The average follow-up period was 7.3 years. The results in these patients were classified according to arbitrarily established criteria, and as many variables as possible were eliminated from the study. Thirteen patients obtained excellent results, 40 good results, and 36 fair results; 26 were therapeutic failures. Significant findings were as follows: Patients with good anamnestic, physical, and myelographic evidence of nerve-root compression obtained better results from disk surgery. Patients who at operation were found to have completely extruded disks obtained better results. The results in women were not significantly worse than in men. In women most of the disk lesions were located at the 4th lumbar interspace. Many of these were also associated with degenerative disks at the 5th lumbar interspace. In men there appeared to be no such predilection for any given interspace. Fourteen (12%) of the 115 patients had recurrences; 10 of these were on the same site as the original lesion, and 4 were on the opposite side. Twenty-eight patients (24.3%) probably should not have been operated on because of degeneration of disk without rupture in 21, because of functional disturbances in 6, and because of later discovered rheumatoid spondylitis in 1.

It seems clear that, if one remembers the past history of low-back pain and sciatica and if one understands the pathological changes in the disk with the resulting altered function of the disk unit, one will limit surgical treatment to those patients who continue to be disabled as a result of pain, or have progressive neurological changes despite adequate conservative therapy. At the present time, the authors believe that spine fusion should be done on patients in whom conservative treatment fails and in whom exploration after careful study reveals only a degenerated disk. Simple disk excision seems adequate in those patients in whom the operative finding is one of definite nerve-root compression. When the original operation fails or the patient has recurrence, fusion should be part of the secondary operative procedure.

Fracture Patterns. A. J. Buhr and A. M. Cooke. Lancet 1:531-536 (March 14) 1959 [London].

The studies described were begun to answer the question: Are fractures in the aged becoming more common? A pilot survey of patients with fractures of the femur from the head to the subtrochanteric level, admitted to the Radcliffe Infirmary, Oxford, from 1938 to 1955 inclusive, was made. The fractures studied did not include pathological fractures (e. g., from carcinoma, Paget's disease, or bone cysts). Of the 1,434 patients, 70% were female and 30% male, and there was a rise in numbers, the cases in the last year being more than 6 times as numerous as those in the first year. A number of factors contributed to this: 1. Admissions to the Radcliffe Infirmary doubled between 1938 and 1955. 2. Oxford was a reception area for evacuees in the 1939-1945 war. 3. An accident service was established in 1941, which tended to attract fractures. 4. The population of Oxford city has increased by more than 12%. Still, a factor of 6 times seemed high. The fractures were then grouped according to the ages of the patients. The figures obtained suggested that a man of over 80 has a liability to fracture the neck of his femur over 30 times as great as a man of under 40, and a woman of over 80 more than 300 times that of a woman of under 40. The magnitude of these factors suggests that the bones must be extremely fragile in the aged, and especially in old women.

It was then decided to study other fractures for which patients received treatment between 1953 and 1957 inclusive. A total of 8,539 fractures, of the upper and lower extremities and of such bones as the clavicle, ribs, pelvis, and spine, were studied. The patients included 5,431 males and 3,108 females. It was found that, on the basis of age and sex distribution, fractures fell into 4 characteristic patterns. The authors designated the first 3 by the letters A, J, and L (because the plotted curves have some resemblance to the shape of these letters); the 4th class they called "composite." Three plotted curves are shown of each of the fracture patterns, and explanations are suggested for the various types of age-and-sex distributions of fractures. Regarding the type A curve, it is pointed out that most of the fractures falling into this group (phalanges of feet and hands and the metacarpals) arise from injuries at work. This is essentially the wage earner's fracture pattern. The male/female ratio is 3.3:1. Type L curve fracture patterns are those involving the shaft of the tibia, clavicle, and lower end of the humerus. These traumatic fractures are common in youth of both sexes, but slightly more so in the male. In age the numbers fall, because severe trauma becomes much less common, and this group comprises bones that presumably do not become appreciably brittle with age. This is essentially the prewage-earning fracture pattern. The male/female ratio is 2:1. Type J curve fractures (femur, pelvis, and upper humerus) require considerable violence in the young, and therefore are more frequent in men than in women. In later life the bones become thin and brittle in both sexes, but more so in women; hence, the increase in both sexes and the crossing of the male and female lines of the graph. This is essentially the postwage-earning fracture pattern. The male/female ratio is 1.1:4.

Regarding the "composite" curve type fractures (fibular malleolus, upper end of radius, and [illegible] end of forearm), the authors say that there is [illegible] no obvious explanation for the patterns where [illegible] are 2 peaks, one in youth and the other in [illegible] both sexes. Fractures of the lower end of the [illegible] arm show a combination of the L pattern for [illegible] and the J pattern for females. The L [illegible] accounted for largely by fracture-separation [illegible] lower radial epiphysis and also [illegible] fractures of the lower end of the radius [illegible] which overlap slightly with fractures [illegible] third of the shaft. The J component [illegible] true Colles fracture. The [illegible] causation of fractures in the [illegible] as well as internal causes. [illegible] causes are the most important [illegible] tors.

NEUROLOGY & [illegible]

Major Post-traumatic Amnesia. [illegible] J.-A. Chavany and F. [illegible] 540 (March 21, [illegible]

Two basic [illegible] ories and their [illegible] ing of memory. [illegible] ly interconnected in [illegible] but they often [illegible] disease or trauma. [illegible] may be [illegible] subsequent [illegible] concerning [illegible] or in [illegible] s extend [illegible] s past and [illegible] e presented [illegible] y accident [illegible] d [illegible] d [illegible] is on the [illegible] p- [illegible] as an emergency case. Examination revealed no apparent wounds and no fracture of the skull. He remained in a coma for several hours and, on regaining consciousness, was found by the physician on duty to have "an extraordinary amnesia bearing on certain remote facts as well as on the circumstances of the accident." No change was observed in the patient's pulse rate, temperature, or respiratory rhythm. The eyegrounds were fairly normal. The initial electroencephalogram showed discrete anomalies involving particularly the posterior part of the 2 hemispheres. The patient was kept under observation for 7 days and then after 2 days at another hospital was discharged and sent home.

The changes in the patient's character—especially irritability and fearfulness—brought about by the accident were striking. Italian by birth, he had always before been physically and psychically healthy, with a happy, enthusiastic disposition. He was fairly well educated, having been a teacher in Italy and then, after coming to France, a specialized worker at the factory where the accident occurred. He had been married 6 months earlier, but did not remember his wife and one night, in a fit of panic, accused her of wanting to kill him. He was brought to the neurosurgical clinic of the Hôpital de la Pitié in Paris for study one month after the accident. His terrified appearance contrasted strangely with his robust, well-built frame. He expressed himself without apparent difficulty but did not speak spontaneously. It was necessary to question him, and his answers, though adequate, were odd. He was disoriented in time and place and did not know his name or the date or place of his birth. He remembered absolutely nothing about his childhood, and doubted whether he had had parents. He knew now that he had a wife but not whether he had any children. He had no recollection of his occupation as a mechanic and even thought he had not been working. Most of the memories stored up before the accident were thus lost, but certain more recent ones were retained; e.g., he was able on that day to give his address.

This massive loss of memory has persisted with variations ever since. Intelligence tests given in March, 1958, revealed the following findings: profound demential regression; impairment of symbolic functions resulting essentially from Wernicke's aphasia; marked apraxic disturbances, especially ideational; total agraphia; difficulties of language comprehension that were hard to evaluate, inasmuch as the patient's mother tongue was Italian and not French; almost complete alexia; profound disturbances of memory; and affective-emotional disturbances of the frontal type: passivity, indifference, unawareness (to a certain extent) of his state; aprosexia; and verbal stereotypy. The patient spends his time at home going from the radio, which is always on, to the window, from which he looks out continually. He has no inclination to work and has lost all initiative. His attention is easily fatigued when he tries to concentrate; his imagination is puerile; and he amuses himself with toys like a child.

The physiopathogenic mechanism responsible for the complete loss of memory in this patient, and the accompanying aphasia and apraxia, neither of which is the result of the other, cannot easily be conceived, but injury to the rhinencephalon, in the broad sense of the term, seems to be the most likely explanation. A physical finding worthy of notice in this connection is a complete loss of smell on the left side, suggesting a contrecoup severance of the olfactory tract.

Epidemic Myalgic Encephalomyelopathy: The Durban Outbreak. R. C. J. Hill, R. W. S. Cheetham and H. L. Wallace. Lancet 1:689-693 (April 4) 1959 [London].

In February, 1955, towards the end of summer in Durban, Union of South Africa, a disease, superficially resembling poliomyelitis, occurred among the nursing staff of Addington Hospital, a general hospital of 850 beds. Since a recognized poliomyelitis epidemic was still in progress, the earlier cases were thought to be atypical examples of this condition, but it soon became evident that this was not so. The disease struck with dramatic suddenness. At first it was confined to nurses living in, but later many of those who lived out were affected. During the month of March sporadic cases were admitted from the city; and this fact, coupled with the failure to incriminate any known toxin, tended to support the theory of an infection. The authors discuss here the 98 cases among the nurses, mention briefly others among the general public, and refer to similar cases reported elsewhere.

No positive evidence was forthcoming which could throw any light on the cause of this outbreak, and its epidemiology remains obscure. The prodromal phase was characterized by severe occipital headache up to 14 days preceding the onset of the acute phase. The acute phase was ushered in by sudden weakness and heaviness in one or more extremities. Stiffness of the neck muscles was associated with severe occipital headache and with weakness of the back and of the abdominal muscles. Paresthesia or severe pain in the affected limb was common. Paralysis was present in at least one extremity. Muscle cramps were common, and occasionally there were bladder symptoms—either dysuria or retention. Symptoms persisted in the majority of patients for 1 to 3 months, and tended to recur on return to duty. The relapse was identical with the initial onset; and in those so afflicted the disablement continued for 6 to 9 months, and then either resolved or persisted as a lack of endurance in the muscles originally involved. Eleven patients are still disabled after 3 years, with complete or partial paralysis of an arm or leg, weakness of a member, or severe back weakness associated with paralysis of a leg.

Low-grade fever, muscular pain, and patchy areas of diminished sensation were some of the physical signs. A predominant feature in all the cases was alteration in either intellect or affect, or both. In the early stages the majority of the nurses showed euphoria. Most of them exhibited inability to concentrate, defective memory, persistent drowsiness, emotional instability, and irritability; yet, at the same time, they displayed an apparent lack of concern as to possible serious sequelae. Special investigations were carried out. While the etiology remains obscure, evidence suggests that the cause is infective. The Addington Hospital outbreak resembled epidemics of myalgic encephalomyelopathy in other parts of the world.

Benign Myalgic Encephalomyelitis: An Outbreak in a Nurses' School in Athens. G. K. Daikos, A. Paleologue, S. Garzonis and others. Lancet 1:693-696 (April 4) 1959 [London].

This paper describes an outbreak of benign myalgic encephalomyelitis in a nurses' school in Athens, Greece, in June, 1958. The main features of the disease were intense muscle pain, slight and transient pareses, extreme tenderness at the periosteum and periarticular tissues, mental disturbances, and objective evidence of diffuse involvement of the central nervous system. Electroencephalographic and electromyographic findings confirmed the impression of involvement of the central nervous system. It is pointed out that the various outbreaks recorded under the name of "benign myalgic encephalomyelitis" or "epidemic neuromyasthenia" have had many similarities but differences in details. The outbreak described here resembles those described by Fog in 1953 and by White and Burtch in 1954. A unique feature of this one was the involvement of joints and periosteum. Although hitherto no viral or bacterial agent has been isolated, the contagiousness of the syndrome strongly suggests an infectious (probably viral) etiology. Its predilection for women (and for nurses) poses interesting epidemiological questions. Continuous and intimate contact, coupled possibly with an infectious focus, is probably necessary.

GYNECOLOGY & OBSTETRICS

Addison's Disease and Pregnancy: Review in Connection with Case Complicated by Myomectomy. S. Schartum. Tidsskr. norske laegefor. 79:335-337 (March 15) 1959 (In Norwegian) [Oslo].

To date, about 80 cases of pregnancy in Addison's disease have been described. The disease usually is manifest at the age of 38 to 40. Hitherto the duration of life has been short because no adequate therapy was available, and many women with Addison's disease were advised against pregnancy, considered a complication dangerous to life. Now pregnancy in Addison's disease is no longer a grave complication. The condition calls for special precautions, but with present-day adjuvants the prognosis should be good. It is important to observe the patient closely and increase the hormone administration before and right after delivery. Cesarean section and other operative interventions at term increase the danger. In the case from Norway reported here, the patient, aged 34 years, became pregnant for the first time a year after the diagnosis of Addison's disease was made. Myomectomy was done about the 5th month of pregnancy, with uneventful postoperative course. Delivery occurred at term. Unimportant fall in blood pressure after delivery was easily controlled with blood transfusion, fluids, and extra hormone administration. The infant did well. The mother's excretion of 17-ketosteroids increased strongly toward the end of pregnancy and fell soon after delivery to values as before.

The Electrophoretic Pattern of Serum Proteins in Toxaemias of Pregnancy. M. K. Krishna Menon, P. D. Radha and N. Ramasamy. J. Obst. & Gynaec. India 9:209-216 (March) 1959 [Bombay].

In a previous study by paper electrophoresis on the protein values in women with eclampsia, the senior author and associates had observed a reduction in the serum protein concentration and particularly a drop in the gamma globulin fraction. Studies were made on 56 women with preeclampsia, who had been pregnant from 34 to 40 weeks and had edema, albuminuria, and hypertension. These were subdivided into 2 grades: Those with systolic pressure between 140 and 180 mm. Hg, with albuminuria of from 1 to 3 plus, and with mild to moderate edema were included in group A; those with systolic pressure above 180 mm. Hg, with varying degrees of albuminuria and edema, and with any of the associated symptoms of headache, vomiting, restlessness, epigastric pain, or visual disturbances were classified as group B. Studies were also made on 42 women with antepartum eclampsia. However, in only 22 cases of preeclampsia, grade A, 7 of preeclampsia, grade B, and 28 of eclampsia were the estimations complete.

On the basis of these studies the authors arrived at the following conclusions: 1. In preeclamptic toxemia and eclampsia there is marked lowering of the total serum protein concentration. This is associated with a fall in the albumin levels and the globulin fractions, and for the latter the statistically significant fall is in the values of the beta and gamma globulins. 2. In threatening eclampsia and in eclampsia the serum protein concentration is higher than that in the milder grades of preeclampsia, but it is lower than that in normal pregnancy. This is perhaps due to hemoconcentration which exists in the severe form of the disease. 3. The serum protein concentration of babies born to mothers with preeclampsia and eclampsia is lower than that of babies born to mothers without eclamptic symptoms. The beta and gamma globulins also show lower values. 4. The variations of the protein concentration 48 and 96 hours after delivery follow a similar pattern to that found after delivery in normal pregnant women. 5. No satisfactory explanation can be offered for the lowered beta and gamma globulin fractions found in preeclampsia and eclampsia.

Absolute Results of Cure in 312 Patients with Carcinoma of the Uterine Cervix (1950 to 1952). J. Spurny and K. Weghaupt. Geburtsh. u. Frauenh. 19:244-252 (March) 1959 (In German) [Stuttgart, Germany].

Of 312 women with invasive carcinoma of the uterine cervix who attended the first gynecologic clinic of the University in Vienna between May, 1950, and December, 1952, 177 were operated on. Of these, 159 patients underwent a radical operation (158 according to Wertheim's technique and 1 according to Schauta's technique); 8 patients were subjected to less radical intervention, the carcinoma being detected on microscopic examination of the operative specimen; and the remaining 10 patients underwent an exploratory laparotomy. Of the 159 patients who had undergone a radical operation followed by postoperative irradiation with roentgen rays, 121 (76.1%) were living and were free of recurrence 5 years after the operation. One hundred thirty-five patients underwent primary combined irradiation treatment with radium and roentgen rays. The 8 patients who did not have a radical operation and the 10 subjected to exploratory laparotomy received subsequent combined radium and roentgen-ray therapy. Of these 153 patients, 54 (35.5%) were living 5 years after the treatment and were free of recurrence. Thus, of the total number of 312 patients, 175 had a 5-year survival, representing an absolute cure rate of 56.4%.

Further Contribution to the Treatment of Toxemia of Pregnancy with Hydergine. E. Lago. Minerva ginec. 11:118-126 (Feb. 15) 1959 (In Italian) [Turin, Italy].

The hypotensive compound, Hydergine, was given to 21 parturients with the pregnancy syndrome of arterial hypertension associated with albuminuria and edema. Eclampsia developed subsequently in 3 patients. Patients with past renal disorders ascribed either to essential hypertension or to other abnormalities were not included in this group. The drug was administered orally and/or intramuscularly to the patients in a moderately severe condition and intravenously to the patients in a severe condition. Thirteen patients had blood pressures of over 160 mm. Hg, and the remainder had lower levels. The hypotensive effect of Hydergine in patients in a moderately severe state, that is, excluding those with eclampsia, was rapid. It lowered the blood pressure by 15/20 mm. Hg of its systolic and diastolic values 7 to 10 minutes after the intramuscular injection of one ampul, which effect lasted for about one hour. In order to maintain the continual effect of the drug, the daily doses consisted of up to 7 ampuls (of 0.3 mg. each) or of 3 ampuls and 3 tablets. The treatment was continued until, and in some instances after, the delivery. The drug also relieved headache, aided diuresis, restored the physiological values of serum albumin, induced a certain degree of normalization of contraction of the uterus and dilation of the cervix, and produced no side-effects. Hydergine was thus an efficacious drug for management of the hypertension of pregnancy (except for those with eclampsia) in this series of patients and in the other groups treated previously.

PEDIATRICS

The Management of Staphylococcal Disease in Infants and Children. M. D. Yow, M. M. Desmond and L. N. Nickey. J. Pediat. 54:409-428 (April) 1959 [St. Louis].

The authors studied antibiotic susceptibility of staphylococcic strains in 204 children with staphyylococcic disease, who were treated at the Jefferson Davis Hospital in Houston, Texas, between 1956 and 1958. The ages of the patients ranged from 12 hours to 12 years. There were 155 babies under 2 months of age, 32 infants from 2 months to 2 years of age, and 17 children who were older than 2 years. Thirty-four of the 155 babies were premature. Sixty-six of the patients had impetigo or conjunctivitis alone; the remaining 138 had more severe involvement. Eighty per cent of the infections were hospital acquired, and 20% were nonhospital acquired. The age of the patient influenced morbidity and mortality. In the 138 patients with serious staphylococcic disease, the mortality rate was 43% in the premature infants, 26% in the full-term newborn infants, 21% in children from 2 months to 2 years of age, and 11.7% in older children. The degree of dissemination was related to the age of the patient, demonstrating inadequacy of host defenses in the young infant.

The management of staphylococcic disease in the young infant differs from that in the older child. All staphylococcic infections must be considered potentially serious in the young infant because of the atypical manifestations and unpredictability of the course of staphylococcic disease in this age group. In the older child superficial infections may be safely treated with local therapy. However, controlled studies are needed to establish the best method of management of infants with superficial infections, such as impetigo neonatorum and conjunctivitis, now that the majority of these infections are due to the highly invasive strain 81. Moderately severe infections, such as deep subcutaneous abscesses, occurring in the older child can be expected to respond to bacteriostatic antistaphylococcic drugs and local care. Subcutaneous abscesses and breast abscesses occurring in the young infant should be treated with a bactericidal antistaphylococcic drug and local care.

The prognosis of severe staphylococcic disease in all age groups is so grave that intensive treatment with a bactericidal antibiotic or the combination of a bactericidal drug and a bacteriostatic drug is indicated. Adequate incision and drainage are essential because of the ability of the staphylococci to remain viable within abscesses. In instances in which it is difficult to insure adequate drainage, it may be advisable to instill a bactericidal antibiotic directly into the infected cavity. In infants, in other individuals who handle infection poorly, and in patients with undrained localized infections, it is necessary to continue therapy for a prolonged period in order to prevent relapses of infection.

Cystic Lesions of the Kidney in Infants and Children. J. B. Arey. J. Pediat. 54:429-445 (April) 1959 [St. Louis].

Although renal cysts of various types are relatively infrequent in early life, their proper identification is important both prognostically and therapeutically. Unfortunately, analogous terms have been applied to quite dissimilar cystic lesions of the kidney, and in many instances the term "polycystic disease" has been employed to refer to any kidney containing multiple cysts. This prompted the author to delineate the various cystic lesions of the kidney encountered in infants and children and to clarify the clinical, roentgenographic, and pathological manifestations associated with specific types of lesions.

Simple renal cysts, perinephric cysts, and multilocular cysts of the kidney are rare in infants and children. They manifest themselves by the presence of an abdominal mass which may be interpreted clinically as a nephroblastoma. The clinical, pathological, and hereditary features of true polycystic disease of the kidneys appear to be distinct from those of renal hypoplasia, and every attempt should be made to differentiate these 2 diseases. The cystic kidneys which may be associated with intrauterine urethral obstruction may represent instances of renal hypoplasia and should not be interpreted as true polycystic disease of the kidneys. Similarly, the unilateral multicystic kidney, which manifests itself by the presence of an abdominal mass, is a form of renal hypoplasia and does not represent unilateral polycystic disease of the kidneys. There is evidence to indicate that infantile and adult forms of true polycystic disease of the kidneys represent 2 independent entities. Further study is necessary before this fact can be established unequivocally.

A Clinical Study of an Exanthem Due to ECHO Virus Type 9. J. W. Geme Jr., J. T. Prince, W. F. Scherer and W. Krivit. J. Pediat. 54:459-467 (April) 1959 [St. Louis].

The authors investigated 13 cases of a summer rubelliform exanthem of which the causative agent was enteric cytopathogenic human orphan (ECHO) virus, type 9. This study included 8 male and 5 female patients, one of whom was an infant, 6 were children between the ages of 1 and 5 years, and 3 were children between the ages of 6 and 10 years; 3 patients were adults. Fever was present in all 13 patients as a symptom either prodromal or concurrent with the rash. At the height of the fever the temperature ranged from 101 to 104 F (38.3 to 40 C), the average elevation being 102 F (38.8 C). The fever persisted from 1 to 8 days, the average duration being 3½ days. Gastrointestinal symptoms were observed in 4 of the 13 patients; all 4 experienced emesis, and one complained of abdominal pain and diarrhea. When these symptoms were actually prodromal to the rash, they occurred up to 5 days before the exanthem appeared. The average duration of this phase was about 1½ days. The exanthem lasted from 1 to 7 days, with an average duration of 2½ days. Of the 13 patients, 11 had a facial rash, but 5 of these exhibited the eruption only on the cheeks. In 9 patients the torso and arms were also involved. Additional physical findings included pharyngitis in 6 patients, conjunctivitis in 4, and cervical adenopathy in 7. Throat cultures obtained from 11 of the 13 patients studied yielded ECHO 9 virus. Positive throat cultures were obtained as late as the 10th day of illness. The incubation period of this infectious exanthem seems to be about one week.

Primary Fibrosarcoma of the Lung in a Young Child: A Case Treated by Lobectomy and Cobalt Therapy. F. S. Gerbasi, A. M. Margileth and R. S. Kibler. J. Pediat. 54:488-495 (April) 1959 [St. Louis].

The authors report a child, aged 2 years and 9 months, with primary fibrosarcoma of the lung who was admitted to the U. S. Naval Hospital in Corona, Calif., in February, 1956. This is the youngest case of this type of sarcoma of the lung ever recorded, and the only case recorded in a child treated by lobectomy and radio cobalt (Co^{60}) therapy. The fibrosarcoma was very anaplastic and responded poorly to the treatment. Excision of the lesion relieved the boy's dyspnea temporarily, but the Co^{60} therapy had little or no therapeutic value. The patient developed extensive metastases and died 13 months after the onset of symptoms.

Intravenous Chloramphenicol in Seriously Ill Infants and Children. B. M. Kagan and N. Felix-Balkcom. J. Pediat. 54:474-483 (April) 1959 [St. Louis].

The authors evaluated treatment with chloramphenicol administered intravenously to 107 children, their ages ranging from 3 days to 13 years; this evaluation had particular reference to clinical effectiveness, patient's tolerance, side-effects, and toxicity. Of the 107 patients, 67 had meningitis, 13 had infectious diarrhea, 10 had respiratory tract infection, 6 had poliomyelitis, 2 had encephalitis, 5 had miscellaneous infection, and 4 had noninfectious diseases. The clinical responses were evaluated in 91 patients; the remaining 16 patients were included for study of tolerance, side-effects, and toxicity, since they had diseases that could not be expected to be influenced clinically by the drug. Twenty of the 107 patients received chloramphenicol by the intravenous route only; 80 received it by the intravenous route first and later orally; 4 received it at first intravenously and later intramuscularly; and 3 received it by the intravenous route first and later by the intramuscular or oral route. The average dosage of chloramphenicol administered intravenously was 68 mg. per kilogram of body weight per day given in divided doses; to the majority of patients it was given every 6 hours. The average total duration of intravenous administration was 3 days. The currently recommended dose administered intravenously is 15 to 20 mg. per kilogram of body weight every 6 hours (or 60 to 80 mg. per kilogram of body weight per day).

Side-reactions and toxic reactions to the administration of chloramphenicol were generally mild and transient. The commonest side-reaction was thrombophlebitis. Diarrhea, skin rash, and transient granulocytopenia occurred in some patients. In one child, who was already critically ill and malnourished, thrombocytopenia and anemia developed. This patient received other drugs simultaneosly, some of which seemed to cause similar reactions. At autopsy, abscesses due to Staphylococcus pyogenes var. aureus were found in all the internal organs. The role of the infection itself in causing bone marrow depression in such a case is difficult to evaluate. To avoid complications due to treatment with chloramphenicol administered intravenously, special care must be exercised in preparation of the "chloramphenicol solution" for intravenous use. The detailed technique of administration to prevent crystallization of the drug has been described.

Of the 91 patients, the condition of 76 improved, but 15 did not respond to chloramphenicol and 7 of them died. Of the 76 improved patients, 43 received chloramphenicol alone, and 33 received chloramphenicol in addition to other drugs administered simultaneously. Of the 15 unimproved patients, 5 received chloramphenicol alone, and 10 received chloramphenicol in combination with other antibacterial drugs given simultaneously. It took from 4 hours to 12 days for the improved patients to become afebrile after the initiation of chloramphenicol therapy. Chloramphenicol given intravenously is therapeutically effective in infections in which there are indications for this drug. It is relatively well tolerated and is an important addition to the regimen for seriously ill patients. However, the intravenous route of administration should be discontinued in favor of the oral route when the patient's condition permits.

UROLOGY

Simple Renal Cysts. F. H. van Gulik. Arch. chir. neerl. 11:57-69 (no. 1) 1959 (In English) [Arnhem, Netherlands].

Simple renal cysts, although comparatively rare, can cause diagnostic difficulties. With the aid of a schematic drawing, the author divides these cysts into 5 different types. Type 1 cyst is not a cyst in the accepted sense; a more precise designation would be "hydrocalyx" or "calyceal diverticulum." The pathogenesis of a hydrocalyx involves factors such as occlusion of the calyceal neck by a small concretion, cicatricial tissue, or dysfunction of the sphincter muscle of the neck. Type 2 cyst is parapelvic; it does not communicate with the renal pelvis. The epithelium that lines this cyst differs from that of the calyx. Pyelogenic cyst (type 3) is assumed by the majority of investigators to be congenital. There is a patent communication with the renal pelvis, and the epithelium does not differ from that of the renal pelvis. Type 4 cyst occurs as a sequel of pyelonephritis. Type 5 cyst is, as a rule, referred to as a solitary or simple cyst.. Its epithelium differs from that of the renal pelvis, and it is virtually never in open communication with the renal pelvis. The term "renal cysts" is generally applied to types 5, 4, and 2. These cysts hardly ever communicate with the renal pelvis. Their epithelium is of the cubical type and, therefore, different from the epithelium lining the renal pelvis.

In commenting on the etiology, the author cites theories advanced by Virchow in 1856, Hildebrandt in 1894, Hepler in 1930, and Kampmeier and McKenna in 1934. Hildebrandt's idea, that the formation of these cysts is due to insufficient communication between nephroblastema parts (glomeruli) and the collecting tubes originating from the Wolffian duct, seems to be the most widely accepted today. Simple renal cysts are most frequently found in the age group 40-60, with some slight female predominance. Cysts may be unilocular and multilocular. The author calls special attention to the solitary multilocular cyst, which must be differentiated from the unilateral cystic kidney. The differentiating characteristics of the solitary multilocular cyst are listed.

In order to obtain information about possible malignant degeneration of renal cysts, an investigation was made, which covered 7,751 patients with urologic disorders and 3,306 autopsy reports. A total of 80 cysts with a diameter exceeding 4 cm. were discovered. Carcinoma was found in such renal cysts in 2 patients. Special mention is also made of an unusually large simple cyst, containing 1.2 liters of fluid, which was attached to the kidney by only a short pedicle. Particularly in the case of cysts of the central part of the kidney, it is often difficult to differentiate between a cyst and a malignant tumor. Aortography may be helpful, since the wall of a cyst is virtually devoid of vessels, whereas a tumor shows vessels and irregularly filled blood spaces. The author feels that surgical inspection is safest; if a cyst is found, it can be opened and resected. Some urologists advocate percutaneous puncture of the cyst under fluoroscopic control. The fluid aspirated may be examined with a view to demonstrating possible tumor cells. Contrast medium could be injected, but the majority of investigators consider this method dangerous. The risks involved are listed.

THERAPEUTICS

Comparative Trial of Isoniazid in Combination with Sulphone or PAS in the Treatment of Acute Pulmonary Tuberculosis in East Africans: A Co-operative Investigation in East African Hospitals and Laboratories with the Collaboration of the British Medical Research Council. East African/British Medical Research Council Sulphone Investigation (1959). Tubercle 40:1-13 (Feb.) 1959 [London].

Pulmonary tuberculosis is a major cause of morbidity and death among Africans. It was estimated that the prevalence of tuberculosis in Tanganyika was 11.5 per 1,000 in 1932, and in Kenya in 1948 and 1949 it was 11.1 per 1,000. An effective combination of drugs that are easy to administer and are cheap is urgently needed for the control of tuberculosis in Africa. Isoniazid is an obvious choice as one drug of such a combination, since it is cheap and rarely toxic and can be taken by mouth. Unfortunately, the other 2 drugs used in the trial in Uganda in 1956, namely, streptomycin and *p*-aminosalicylic acid (PAS) have disadvantages for widespread use in Africa. Streptomycin has to be given by injection and is expensive; PAS is expensive and bulky in therapeutic doses and may have unpleasant side-effects. The sulfones are cheap and relatively nontoxic and can be taken by mouth. They have been used in Africa for the treatment of leprosy, and, since they had proved active in experimental tuberculosis and had been reported as having some antituberculous effect in man, it was decided to use diaminodiphenylsulfone (DDS) in combination with isoniazid.

East African patients with acute extensive bilateral tuberculosis were treated in the present trial in hospital for 6 months. Two treatments were compared, isoniazid plus DDS and isoniazid plus PAS. The regimen for each patient was decided by a random procedure. Of 146 patients first selected for treatment, 29 were excluded from the final analysis for various reasons. Of the 117 patients, 61 belonged to the DH series. They received 200 mg. of isoniazid daily in 2 equal doses by mouth, with an interval of about 12 hours, plus 100 mg. of DDS daily in 1 dose by mouth. The remaining 56 patients, called the 10-PH series, received daily 200 mg. of isoniazid, plus 10 Gm. of the sodium salt of PAS, in 2 equal doses by mouth, with an interval of about 12 hours. The 2 series of patients were clinically, roentgenographically, and bacteriologically similar at the start of treatment.

No troublesome toxic effects were encountered. At the end of 6 months the average weight gains were 18.3 lb. for the DH patients and 22.1 lb. for the 10-PH patients. Among the febrile patients, 64% in the DH series and 90% in the 10-PH series were afebrile at 6 months. There were substantial improvements in sputum character, sputum volume, and erythrocyte sedimentation rate at the end of 6 months, all to a similar extent in the 2 treatment series. Changes in cavitation showed no difference between the series. There were no deaths in either series during the 6-month period. At the end of 6 months 71% of DH patients and 96% of 10-PH patients were bacteriologically negative on a single direct examination; 58% of DH patients and 90% of 10-PH patients were negative on culture. Isoniazid resistance was found at 6 months in 17 of 18 positive cultures from DH patients and in 3 of 5 from 10-PH patients. While DDS proved ineffective as a substitute for PAS in preventing the emergence of isoniazid resistance, clinically the combination isoniazid plus DDS was only slightly inferior to isoniazid plus PAS over a period of 6 months. However, because of uncertainty as to whether DDS had any clinical effect, the trial cannot be regarded as providing information on the relative efficacy of isoniazid alone and isoniazid plus PAS in acute bilateral pulmonary tuberculosis. A further investigation to compare these regimens directly is in progress in East Africa.

A Controlled Trial of Various Forms of Physiotherapy in Arthritis. D. E. Hamilton, E. G. L. Bywaters and N. W. Please. Brit. M. J. 1:542-544 (Feb. 28) 1959 [London].

One hundred thirty-one outpatients with either rheumatoid arthritis, involving the hands or knees, or with degenerative joint disease, involving the knees, were subjected to a therapeutic trial in the physical therapy department of Hammersmith Hospital in London. Instead of comparing 4 separate groups of patients treated in different ways, each of the patients was treated with each of 4 treatments, so that each patient served to some extent as a contratest on himself. The treatments selected for comparison consisted of (1) short-wave diathermy given for 20 minutes 3 times a week, (2) infrared radiation, for 20 minutes 3 times a week, (3) faradism to the quadriceps of patients with involvement of the knee, for 20 minutes 3 times a week, or wax treatment of patients with involvement of the hands, for 20 minutes 3 times a week, and (4) in addition, patients were given what was called "cold short-wave diathermy," administered in the same way as ordinary short-wave diathermy but without turning on the current. This 4th method of treatment served as a contratest, and the patients were given a warning that they would probably not feel any heat. Sixty-seven of the 131 patients attended for the full 5-month course.

The results showed that, although in each of the 3 diagnostic categories there was some improvement after treatment compared with the patient's state before treatment, this occurred more commonly with the first treatment, whatever that consisted of, and that, when short-wave diathermy, infrared radiation, and faradism or wax treatment were compared with a dummy exposure to short-wave diathermy, no significant difference was seen. This means that, if there was a difference between treatments, it was too small in relation to the variability of the group and of the measurements to be distinguishable in this number of patients from that due to chance variability. It must be remembered that all patients were on a good basic regimen of exercises, analgesics, splintage, and encouragement, and it seems possible that the general improvement noted could, in fact, be due to this basic regimen.

Treatment of Terminal Leukemic Relapse by Total-Body Irradiation and Intravenous Infusion of Stored Autologous Bone Marrow Obtained During Remission. J. J. McGovern Jr., P. S. Russell, L. Atkins and E. W. Webster. New England J. Med. 260:675-683 (April 2) 1959 [Boston].

Two girls, aged 2 and 8 years, and a 4-year-old boy with acute lymphocytic leukemia in terminal relapse were treated with total-body irradiation (570 to 600 r), followed within one hour by the administration of preserved autologous bone marrow that had been obtained from the patients during a previous period of remission from leukemia and had been stored at —70 C in 15% glycerol. The boy died 9 days after irradiation, and leukemia was found to be still present on autopsy. The 8-year-old girl died 23 days after irradiation, and no evidence of leukemia or repopulation of the bone marrow was found at autopsy. The third patient showed recovery of normal marrow within 17 days after irradiation, with a clinical and hematological remission; the rapidity of recovery of normal bone marrow and peripheral blood after an irradiation exposure in the potentially lethal range, according to data from the atomic bomb casualties in Japan, suggested that the attempted bone marrow autograft was successful. These observations suggest that further investigation of this method of therapy in leukemia is warranted.

Chlormerodrin: Clinical Effectiveness and Absence of Toxicity in Congestive Heart Failure: Report of a Four-Year Study. W. A. Leff and H. E. Nussbaum. Brit. M. J. 1:883-889 (April 4) 1959 [London].

The authors report on 26 men and 22 women, between the ages of 29 and 80 years, in chronic congestive heart failure, who were maintained in a state of cardiac compensation with chlormerodrin (Neohydrin), an orally administered organomercurial agent, over a 4-year period. All the patients received maintenance doses of digitalis and were advised to stay on a salt-free diet. An additional 5 patients treated with chlormerodrin during the 4-year period had gastrointestinal disturbances manifested by nausea, vomiting, and diarrhea; these patients were regarded as failures because of their intolerance to the drug and were not included in this report. Of the 48 patients, 39 had previously received meralluride (Mercuhydrin) by the parenteral route for periods ranging from 6 months to 10 years before the institution of oral treatment with chlormerodrin; the remaining 9 patients had never received organomercurial agents by the parenteral route before the treatment with chlormerodrin. Combined total dosage of orally and parenterally administered mercury ranged from 6,240 to 78,560 mg. per patient, with no clinical evidence of renal toxicity due to the organomercurial agents. Renal function was tested in every patient by means of urinalysis and tests for urea nitrogen, nonprotein nitrogen, and creatinine. Urea clearance tests were done in 17 patients. The sole abnormalities detected were occasional albuminuria in 7.

Eight patients died after 7 to 33 months of treatment with chlormerodrin. None of these deaths were related to toxicity of the diuretic. Autopsy was performed on 3 of the 8 patients; there was no gross or microscopic evidence of renal damage due to mercury. Tissue analysis for mercury revealed a small mercurial content in the kidneys and infinitesimal amounts in heart muscle, liver, spleen, and large intestine. Chlormerodrin showed no evidence of renal toxicity over a 4-year period. Most so-called toxic reactions to organomercurial diuretic therapy can be eliminated by proper control of therapy in sensitive patients.

QUESTIONS AND ANSWERS

SOURCE OF ESTROGENS

To the Editor:—*It is said that there is more estrogen outside the ovary than within the ovary. Is this an authentic statement?*

W. J. Tucker, M.D., Ashland, Wis.

Answer.—The major source of estrogen is within the ovaries and not from areas outside the ovaries. In women the elaboration of the biologically active estrogens, namely, estrone, estradiol, and estriol, reaches two peaks of excretion, one at about the midmenstrual period and the other about one week premenstrually. Brown found the average peaks in seven women to be 20.1 mcg. of estrone midmenstrually and 11 premenstrually. For estradiol it was 9.4 mcg. midmenstrually and 4.7 premenstrually. For estriol it was 34.1 mcg. midmenstrually and 24 premenstrually. After irradiation of the ovaries these dropped to 6 mcg. of estrone, less than 1 of estradiol, and 6 of estriol.

Strickler and associates found an average of 3.4 mcg. of estrone, 0.7 of estradiol, and 2.7 of estriol in the midmenstrual period and an average of 8.5 mcg. of estrone, 0.5 of estradiol, and 12.3 of estriol in the premenstrual period in the female. The excretion in the pooled urine of men was 0.5 mcg. of estrone, 0.4 or less of estradiol, and 1 of estriol in 24 hours. The adrenal gland, and, to a slight extent, the testes are the other sources outside of the ovaries for the presence of estrogen, but the main source of estrogen is the ovaries.

POLIOMYELITIS VACCINE

To the Editor:—*Should patients under 40 years of age whose hospitalization period will be from six months to several years, such as those having tuberculosis and neuropsychiatric conditions, be given poliomyelitis vaccine on request?*

E. K. Disney, M.D., Dawson Springs, Ky.

Answer.—Such patients may, on request, be given poliomyelitis vaccine, provided the physician in charge of the case deems the patient's condition warrants it. It is important that patients suffering from such chronic diseases as tuberculosis or neuropsychiatric conditions be protected against poliomyelitis if there are no contraindications. A case of poliomyelitis superimposed on an existing chronic disease might prove to be a serious complication. Few, if any, severe reactions or side-effects have been reported from the use of Salk poliomyelitis vaccine.

HYPNOSIS FOR ELEPHANTIASIS

To the Editor:—*Is hypnotism ever used as a treatment in elephantiasis, and if so, when?*

Ralph M. Crowley, M.D., New York.

Answer.—Hypnosis is not an indicated treatment for elephantiasis, although in the 1840's James Esdaile used hypnotic anesthesia or mesmerism, as it was then termed, to enable him to remove surgically certain large tumors caused by this disease. A possible use of hypnosis in elephantiasis would be no more than that of enabling the patient as a personality to adjust psychologically to the problems occasioned by his illness.

RENAL AGENESIS

To the Editor:—*The first-born infant of a patient was a normal female child. On her two subsequent deliveries she gave birth to boys who lived only a few hours. Autopsies on both boys revealed complete renal agenesis. This patient is considering the possibility of becoming pregnant again. What are her chances of having another defective infant?*

Leonard Rosenfeld, M.D., Ringoes, N. J.

Answer.—The available literature about renal agenesis does not provide the evidence necessary for an adequate answer to this question. The pregnancies subsequent to that with an affected child are seldom reported, and details on other relatives are scanty. Furthermore, similar cases in a family could easily be lost from analysis unless autopsies had been performed, permitting an accurate diagnosis. There have been at least three families with two affected children in each. On the other hand, there are reports of normal children born after a child with renal agenesis. In 1952, Levin described a pair of twins (considered monozygous) with one affected and one normal, but this case does not rule out the possibility of a genetic component. There is a preponderance of affected males (about three males to one female), but this should not be described as "sex linkage."

In the absence of precise data, one can at least set up limits for an estimate of the risk of another defective child. The chance that this woman's next child will have renal agenesis is almost certainly higher than that for the general population, but it

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The answers here published have been prepared by competent authorities. They do not, however, represent the opinions of any medical or other organization unless specifically so stated in the reply. Anonymous communications cannot be answered. Every letter must contain the writer's name and address, but these will be omitted on request.

should not be higher than 25%. This figure is based on the possibility that the condition is behaving as a recessive genetic trait. Probably the risk of a repetition is much less than 25%, but how much less is not known. It may help to have the following additional information: Are the patient and her husband blood relatives? In the parents and their relatives are there any cases of deformities involving the ears, lower extremities, genital organs, or urinary system?

HYPOGLYCEMIC SYNCOPE

To the Editor:—*Several times in the past few months, lay people have been encountered who have the impression that a diabetic taking insulin is subject to sudden loss of consciousness without warning. In the book "How to Live with Diabetes," by Dolger and Seeman (New York, W. W. Norton & Co., Inc., 1958, p. 112), is this statement: "Diabetic coma is slow in onset and may take 24 hours or more to develop. But shock can literally happen in an instant. A diabetic may seem perfectly normal one moment, be unconscious the next." The context is such that the two sentences pertaining to shock and unconsciousness refer to insulin reactions. Such a dramatic episode has not been encountered by this writer since insulin first came on the market, about 36 years ago. Please comment on the above statement. It is important because some persons advocate prohibiting diabetic persons from operating motor vehicles.*

John H. Schaefer, M.D., Los Angeles.

Answer.—Unfortunately, it is true that certain diabetics who take insulin may lose consciousness due to hypoglycemia without recognizing the usual warning symptoms. As a rule, close questioning will reveal that a warning, such as hunger, tremor, or sweating, may have been present but not appreciated. Patients often forget that they had such a premonition. In this they resemble patients who have coronary disease for years before a final coronary occlusion occurs. Accidents on the highways caused by such insulin reactions have been extremely rare. Indeed, studies now in progress indicate that diabetic patients who have received proper instruction in the use of insulin and diet have fewer accidents than their nondiabetic spouses, who also drive automobiles. In Holland, a study of 73,413 automobile accidents showed that only 5 per 100,000 occurred when a diabetic driver had hypoglycemia (Gerritzen, *Zentralbl. verk. Med.*, pp. 165-168, 1956). Onset of coma is slow, in contrast to symptoms in an insulin reaction which come on usually within a shorter period. A person who has three regular meals, a snack in the morning, and one or two snacks in the afternoon, depending on exercise, and a little snack on retiring (with or without glycosuria at that time) rarely has a reaction. Good judgment is still required for the proper use of insulin.

BLOOD GLUCOSE CURVES

To the Editor:—*Please interpret the following blood glucose curve in terms of the possibility of functioning tumor of the pancreas. Also, what other investigations are indicated? A 52-year-old man has had blackouts for several years. Physical findings are normal. His fasting blood glucose level (enzymatic test) was 90 mg. per 100 ml.; one hour after taking 100 Gm. of glucose, 150 mg.; two hours after, 90 mg.; three hours after, 93 mg.; and four hours after, 30 mg. At this point there were no symptoms.*

M.D., New Jersey.

Answer.—The blood sugar values recorded for the glucose tolerance test are those of a normal curve except the one for the fourth hour. This value should be considered in error until verified, especially since the patient had no symptoms of shock. This is the only value suggesting hyperinsulinism. Paroxysmal attacks that resemble insulin shock, that occur in about 20% of patients with islet cell tumors of the pancreas, especially with excessive fatigue or during fasting, are associated with blood sugar concentrations of 50 mg. per 100 ml. or less. These attacks are relieved promptly by the ingestion of glucose.

MULTIPLE LIPOMATOSIS

To the Editor:—*What would cause a rash of fatty tumors developing at an alarming rate in a young man 25 years of age?* *M.D., Rhode Island.*

Answer.—Multiple lipomatosis is an infrequently seen condition in which multiple fatty tumors occur on symmetrical portions of the arms and body. These appear as smooth masses in the subcutaneous tissues and may be somewhat tender, particularly if there is an increase of fibrous tissue in the tumors (fibrolipoma). There is no known cause for the appearance of these tumors, and efforts to link their appearance to disorders of fat metabolism have not been successful. The treatment is excision of any symptomatic tumor with the patient under local anesthesia.

DENTAL X-RAYS FOR CHILDREN

To the Editor:—*Is it necessary to x-ray the teeth of children who have a routine dental check once a year?* *M.D., Massachusetts.*

Answer.—A dental patient should be exposed to the least amount of x-radiation that will produce the roentgenograms necessary for the evaluation of his oral health. The decision that a practitioner of the healing arts must make is whether the benefits to be derived from the roentgenogram outweigh the possibility of potential harm. This, then, is a question of professional judgment, and the well-being of the patient is the paramount issue. Extensive routine roentgenographic surveys are seldom indicated and should be avoided. Special care should be used with children. Only a few exposures are necessary for the child. Pregnant women should not be subjected to extensive roentgenographic exposures.

The aforegoing statement also presumes that the exposures are made with a modern dental x-ray machine or with a modernized older x-ray machine, properly filtered and collimated, and that fast films are used and slow developing techniques practiced. These precautions greatly reduce the amount of radiation received by the patient. For a clear exposition of the use of x-rays in the healing arts, send 25 cents to the American College of Radiology, 20 N. Wacker Dr., Chicago 6, or to the order department of the American Dental Association, 222 E. Superior St., Chicago 11, for the 30-page booklet, entitled "A Practical Manual on the Medical and Dental Use of X-rays with Control of Radiation Hazards."

PERSISTENT ALBUMINURIA

To the Editor:—*A 65-year-old retired man, who weighs about 200 lb. (90.7 kg.), in spite of taking a low-protein and low-sodium diet has for the past two or three years continuously had about 2+ albumin in his urine. His nonprotein nitrogen level is 49.5 mg.%; erythrocyte count 4,290,000 per cubic millimeter; hemoglobin level 11 Gm.%; leukocyte count 6,450 per cubic millimeter, with 32% lymphocytes, 4% eosinophophils, 63% segmented cells, and 1% nonsegmented forms; hematocrit value 39%; glucose level 111 mg.%; and serologic test for syphilis nonreactive. There is no sugar or acetone in the urine but many pleomorphous bacteria. Erythrocytes and epithelial cells in the urine are rare. The average blood pressure is 220/120 mm. Hg when he is not taking an antihypertensive drug. The heart is essentially normal, and he has no edema. The patient has been periodically taking several urinary antiseptics and antibiotics, such as sulfasoxazole and the tetracyclines, but these have not affected his proteinuria. What other measures could be used to decrease this albuminuria?*

Julian Movchan, M.D., Oakwood, Ohio.

Answer.—Moderate albuminuria, substantial azotemia, and mild anemia suggest moderately advanced, bilateral renal disease. The heavy bacilluria suggests infection and stasis and indicates a detailed urologic survey under appropriate antibiotic control, as determined by preliminary culture and sensitivity studies of the infecting organism(s). Retrograde urography and other studies may establish the process as primarily pyelonephritic. The possibility that the infection has been implanted on damage caused by chronic glomerulonephritis, nephrosclerosis, or arteriosclerosis of major renal vessels exists, and unexplained functional or structural differences between the two kidneys would suggest the further desirability of renal angiography. The proteinuria, presumably of the order of 1 to 3 Gm. daily, is not harmful as such. It presumably reflects "leaky" nephrons in areas of damage and scarring and would not be expected to respond to antibiotics. Appropriate measures are those (urologic diagnosis, courses of therapy with selected antibiotics, and, perhaps, antibacterial medication) which would resolve existing infection and prevent further renal damage. The antihypertensive drugs, to which the patient seems to respond, would also be indicated, with due precautions in view of the azotemia.

MAMMARY CARCINOMA IN SITU

To the Editor:—*A 42-year-old woman had one breast removed for a single clinically demonstrable adenocarcinoma. Histological examination of the breast after removal showed many nonmetatastic areas of carcinoma in situ. These areas were not demonstrable clinically. In view of the fact that the other breast may contain the same in situ lesions, should anything be done with the other breast at present or should one wait for a clinically demonstrable tumor?*

M.D., New York.

Answer.—The situation described is a bit unusual, in that one does not often receive a report of multiple areas of carcinoma in situ in breast tissue. If this pathological opinion has been verified by consultation, it would seem wise to do a simple mastectomy on the remaining breast, since it may well contain similar areas.

SCABIES

To the Editor:—*Scabies has occurred in patients on several wards at this hospital. What is the best procedure to cure the condition and prevent reinfestation?*

M.D., Virginia.

Answer.—An emulsion of either 20% benzyl benzoate or 1% gamma benzene hexachloride rubbed gently but thoroughly into the skin over the whole body and left on continuously for 24 hours is almost always effective in killing not only the mites which cause scabies but also their ova deposited in the skin. In adults the head and neck from the collar-line up need not be treated. It is easy to overlook signs of the disease in early infestations, and itching may not develop immediately. Consideration might, therefore, be given to treating all the patients on a ward at once. A more conservative approach would be to treat all the known or suspected cases at one time and then move them to a separate "clean" ward or segregate them in a portion of the ward if this is feasible. Close observation should then be kept on the remaining nontreated patients for signs of the disease.

All of the personnel in contact with the patients should receive the same careful examination as the patients. Any suspected of having the disease should be treated concurrently. Suspicion should extend to the families of any infested personnel. Clothing and bedding should be sterilized. Usual hospital laundering or dry cleaning procedures should be adequate to kill parasites or ova. Thorough slow ironing or hot-iron pressing should also suffice After treatment, a bath should be given and fresh clothing and bedding provided. Postscabietic dermatitis and itching should be treated with appropriate soothing topical medication. Complicating excoriation and secondary infection may also require special care.

SEDATION BEFORE ELECTROENCEPHALOGRAPHY

To the Editor:—*The use of chloral hydrate for sedation of patients who are to undergo electroencephalography has been considered. What amount per pound of body weight should be given? What contraindication would there be in using the drug? Is it affected in any way by the use of tranquilizers?*

Frank A. Andrews, M.D., Coldwater, Mich.

Answer.—A number of laboratories have used chloral hydrate for several years to induce sleep for the purpose of electroencephalography. This consultant rarely uses it alone, since a more desirable state of sleep can be obtained by combining it with secobarbital. For adults who weigh about 150 lb. (68 kg.), 1 Gm. of chloral hydrate and 200 mg. of secobarbital are given. For children with weights between 50 and 75 lb. (22.7 and 34 kg.), 0.5 Gm. of chloral hydrate and 50 mg. of secobarbital are used. If used alone, the chloral hydrate dose should be increased 50%. It is not used in the presence of severe hepatic or renal disease. Small amounts of such tranquilizers as meprobamate have not interfered with its use, but this consultant has had no experience with large doses of such drugs. The chloral hydrate is given in the form of a syrup containing 1 Gm. in 4 cc. No sedation is used for children under 6 months of age. Suppositories containing 0.3 Gm. of chloral hydrate and a suppository containing 60 mg. of secobarbital are used in children according to this formula: 6 months to 1 year, one-half of a chloral hydrate suppository; 1 to 2 years, two-thirds of a suppository; 2 to 3 years, one whole suppository; 3 to 6 years, one whole suppository and one suppository of secobarbital; and 7 to 10 years, one-half teaspoonful of the syrup (500 mg. of chloral hydrate and 50 mg. of secobarbital).

ADRENOCORTICAL HYPOFUNCTION

To the Editor:—*A 37-year-old woman began treatment in September, 1956, with a previous diagnosis of adrenocortical hypofunction. Urinary steroid determinations had not been performed. She has been treated with an average of 37.5 mg. of cortisone and added salt daily. She would like very much to have studies repeated to the extent of having steroid bioassays performed. What could be done in such an instance to provide minimally reliable information as to the potential ability of the adrenal glands to function in response to endogenous ACTH? Could fludrocortisone be used to maintain the patient's needs so as not to interfere with hormone bioassay results? Assuming any adrenal hypofunction now present to be due to suppression by the administered cortisone, what minimal period of time would be necessary in order to allow sufficient recovery of the glands so that steroid determinations would be reliable?*

M.D., Virginia.

Answer.—Except in patients in whom the clinical findings are classic and who have been observed in a state of frank adrenocortical insufficiency and have made a definite response to specific therapy, it is desirable to confirm or exclude the diagnosis of adrenocortical hypofunction by appropriate laboratory tests. These include, particularly, those involving determination of the response of the adrenal cortex to stimulation with ACTH. In the case in question, the patient may be maintained with 0.1 mg. of fludrocortisone by mouth daily so as to cause minimal inference with determinations of steroid levels in the plasma and urine. Because of possible adrenocortical suppression by antecedent treatment with cortisone, a strong stimulus with ACTH is desirable and it is suggested that she be given 40 mg. of long-acting ACTH twice daily for four days after base-line determinations of the plasma corticosteroid and urinary 17-ketosteroid and corticosteroid levels. The same determinations are then carried out throughout the period of ACTH stimulation, or at least on the last two days. If the patient actually has adrenocortical hypofunction, there should not be a significant increase in plasma or urinary steroid levels in response to ACTH. It is difficult to estimate how much time would be necessary for recovery from suppression of the adrenal cortex by previous treatment with cortisone, but this is not pertinent in the present case, as the diagnosis can be established or ruled out relatively quickly by the procedure outlined above.

HYPOPARATHYROIDISM AFTER THYROIDECTOMY

To the Editor:—*If typical findings of severe hypoparathyroidism are seen after thyroidectomy and no evidence of removal of the parathyroids is reported by the pathologist, could a latent type of parathyroidism have been present preoperatively or would it be assumed that this was a calculated risk with thyroidectomy due to impairment of the parathyroid blood supply? Could the doctrine of* res ipsa loquitur *be involved here? Even though clinics in which many thyroidectomies are performed report a definite incidence of hypoparathyroidism, would this be considered evidence of carelessness on the part of the surgeon?*

William F. Quinn, M.D., Los Angeles.

Answer.—It is doubtful that a latent type of parathyroidism existed preoperatively, and one must assume that the postoperative hypoparathyroidism was the result of the operation. This is a calculated risk in any thyroidectomy, particularly those in which the thyroid gland is difficult to remove. No mention was made of whether the whole gland was taken out or only partially removed. Also no mention was made relative to the type of operation. Idiopathic hypoparathyroidism is a relatively rare disease (Naef and Adle, *Ann. Int. Med.* 50:495, 1959).

PROTEIN-BOUND IODINE DETERMINATIONS

To the Editor:—*Relative to the artefacts produced by various medicaments and x-ray contrast mediums in the performance of protein-bound iodine determinations, please state the length of time during which the drug must be withdrawn, or length of time after diagnostic procedure before such determinations can be expected to be accurate. For example, how long after inorganic iodine therapy, after giving the various antithyroid drugs, and after doing gallbladder x-rays can the determination be performed with accuracy?*

M.D., Pennsylvania.

Answer.—Accurate protein-bound iodine determinations can be expected one week after discontinuing treatment with Lugol's solution (Rapport and Curtis, *J. Clin. Endocrinol.* 10:735, 1950) and four days after withdrawing a cough medicine containing 786 mg. of iodine per ounce in the form of calcium iodide (Fitzsimons and Norman, to be published). A vitamin preparation containing 0.5 mg. of iodine per capsule, even though taken liberally, will not result in an elevated protein-bound iodine level, according to Fitzsimons and Norman. Iopanoic acid and iodoalphionic acid may result in inaccurate protein-bound iodine findings for as long as one year after cholecystography (Fitzsimons and Norman; Riggs, *Tr. Am. A. Study Goiter,* p. 137, 1947; Slingerland, *J. Clin. Endocrinol.* 17:82, 1957). Accurate protein-bound iodine determinations may be expected two to four weeks after the use of iodopyracet compound or methylglucamine diatrizoate for urograms (Fitzsimons and Norman; Man and Peters, *J. Lab. & Clin. Med.* 35:280, 1950). Iodized oil, when used for bronchograms, may remain as a contaminant in plasma for eight months to two years (Fitzsimons and Norman; Man and Peters) and, when used for myelograms, may be present in plasma for as long as five years. About one month should elapse after discontinuing the use of antithyroid drugs, such as propylthiouracil, before attempting to establish the status of the thyroid gland with protein-bound iodine determinations.

PROTHROMBIN TIME

To the Editor:—*In many patients who are taking bishydroxycoumarin, in spite of use of the prescribed dosage the prothrombin time shows unpredictable changes upward or downward. Exposure to southern climate in the winter (a trip to Florida or the Bahamas) shortens the prothrombin time. Is any work being done to determine whether sunlight, extra vitamin C intake, extra vitamin K intake, or other factors influence the effect of bishydroxycoumarin on prothrombin time?*

W. Scheffler, M.D., Merchantville, N. J.

Answer.—Sunlight and vitamin C may both benefit the general health of the patient. The latter may have some effect in the maintenance of the integrity of the capillaries and thus prevent bleeding in case of an overdose of bishydroxycoumarin. There is probably no effect on the prothrombin time or on the response to the anticoagulant. Vitamin K is a specific antidote for bishydroxycoumarin; its administration will raise the lowered plasma levels of prothrombin, and an increased dose of bishydroxycoumarin will be needed for the maintenance of a therapeutic level of the prothrombin time. Physiological mechanisms concerned with the absorption of vitamin K and the production of prothrombin in the liver from this vitamin are important considerations with respect to the response of the patient to bishydroxycoumarin. Hepatic disease interferes with prothrombin production. Poor secretion of bile acids will interfere with vitamin K absorption, as will change in the intestinal flora seen occasionally with chemotherapeutic agents. Aspirin will enhance the response to bishydroxycoumarin. At present, investigations are under way which link the adrenal response to stress to an increased response to anticoagulants. Increased amounts of vitamin K may be toxic due to the chemical structure and there may be some overproduction of prothrombin and a slight hypercoagulability of the blood, but this is unlikely.

POTASSIUM EXCRETION

To the Editor:—*Please give a simple office procedure to determine potassium excretion. Would the urine chloride examination be of value?*

George Hafitz, M.D., Trenton, N. J.

Answer.—Two current methods are available for determining potassium excretion in the urine. The first is accomplished by means of the flame photometer and the other by modifying one of the methods with tetraphenylboron used as described for serum potassium (Sunderman and Sunderman, *Am. J. Clin. Path.* 29:95, 1958). Neither method is simple or suitable for office practice. Determination of urinary chlorides will furnish no results on which to calculate the excretion of potassium.

DRINKING LEMON JUICE

To the Editor:—*Is it advisable to drink the juice of a lemon daily?*

Charles H. Cherry, M.D., Long Beach, Calif.

Answer.—According to Stafne and Lovestedt (abstracted, *J. A. M. A.* 133:1218 [April 19] 1947), the use of lemon juice as a daily drink in any appreciable concentration should be discouraged. These authors reported that in a series of 50 patients who were using lemon juice continually there was evidence of dissolution of dental structure. While the daily use of lemon juice has been advocated by many persons, an adequate amount of vitamin C can be had without resorting to the improper use of lemon juice, in view of its solvent effect on the teeth.

MYDRIATICS

To the Editor:—*Please supply a list of mydriatics. The following report has been received from an ophthalmologist: "After mydriasis with 10% phenylephrine, anterior and posterior cortical changes were present in both eyes with spokes into the pupillary region." This seems to be a rather strong solution.*

Joseph Halton, M.D., Sarasota, Fla.

Answer.—The pathological changes in the lens which the ophthalmologist described were revealed when the pupil was dilated by the 10% solution of phenylephrine and were not induced by the solution. The osmotic pressure of such a solution is equal to only about three times that of a 0.9% sodium chloride solution and produces only a slight transient irritation until the tears dilute it. It is wise to keep all solutions which are dropped into the eye as nearly isotonic with the tears and as near the pH of the tears (7.4) as possible, particularly if the solution must be used repeatedly and over long periods of time. This is not always practicable. For example, epinephrine and its more powerful relative phenylephrine precipitate out of an alkaline solution and will not remain stable at a pH above 5. The degree of dissociation of the salt and the nature of its ions determine the pH and to some extent the osmotic pressure, and these quantities can often be modified by suitably buffering the vehicle. The most important mydriatics are atropine, homatropine, scopolamine, eucatropine, epinephrine, ephedrine, phenylephrine, hydroxyamphetamine, and cocaine. The first three of these are also cycloplegics.

MIST-O-METER MIXTURE

To the Editor:—*Asthmatic patients at this hospital have been treated with a Mist-O-Meter mixture, and one of the staff members questioned whether the alcoholic solution was sufficiently irritating to the bronchi to cause them to develop an increased exudate. Please supply information on this. Are any nonalcoholic liquid preparations used in the same way?*

M.D., North Dakota.

Answer.—The 35% ethyl alcohol content of the Mist-O-Meter mixture might be irritating to the bronchial mucosa if the Mist-O-Meter were used frequently. It probably would not result in an increase of exudate. Isoproterenol is available in saline solution in 1:200 and 1:100 concentrations for use with standard nebulizers.

TRANQUILIZERS AND OPERATION OF AUTOMOBILES

To the Editor:—*In* The Journal, *July 6, 1957, page 1171, it is stated in reference to tranquilizing drugs: "A direct study of performance capacity . . . showed no decrease from normal after twice the usual dose of meprobamate. These studies of acute action are now being extended to chronic use, but results are not yet available." Have these investigations been completed, and, if so, what are the findings?*

Curt Schwietzer, M.D.
Berlin-Dahlem
Germany.

The above comment was referred to the consultant who answered the original question, and his reply follows.—Ed.

To the Editor:—*Further studies show that normal subjects experience no adverse effects with long-term administration of either meprobamate or prochlorperazine. Some current work suggests a slight decrement in performance in anxious subjects under long-term meprobamate administration similar to those reported by Loomis and West* (Pharmacol. & Exper. Therap. 122:525, 1958). *Whether the effect in such subjects is of a magnitude of any practical importance has not been established.*

WASHINGTON NEWS

Fourth Poliomyelitis Vaccine Shot Proposed . .
Live Poliovirus Vaccine . .
Increased Research Money Challenged . .
Air Pollution Control Supported . .
International Medical Cooperation . .

ADVISORY GROUP RECOMMENDS FOURTH POLIOMYELITIS VACCINE INJECTION

An advisory committee of the U. S. Public Health Service formally recommended a fourth, or booster, injection of Salk poliomyelitis vaccine for infants and adults under 40 years of age. The PHS previously had not taken an official stand on the fourth injection, on the grounds that the public should be encouraged to receive three injections first.

The advisory committee proposed a basic schedule of four injections for infants under 6 months of age and for all adults under 40 who have completed the basic schedule of three injections at least one year before, "and especially if several years have elapsed since completion of the basic series."

The committee, composed of representatives of the American Medical Association, the Defense Department, the PHS, and other experts, including Dr. Jonas Salk, said that vaccination of persons over 40 years of age with a fourth injection can be beneficial, but is "less urgent since polio occurs less frequently in older individuals."

The fourth injection was recommended for persons traveling to areas where the incidence of the disease is high; in areas where sanitation is poor or local epidemics are starting; and for persons whose children are about to enter school. Pregnant women should receive a fourth injection prior to the poliomyelitis season "for the vaccine not only provides added protection against polio for the mother but also provides a passive immunity to the unborn baby."

The booster doses, the committee held, are "expected to increase antibody titers in persons in whom the antibody levels have fallen or in whom the initial antibody response was weak, thereby providing possible added protection. . . ." Those vaccinated with three injections have maintained a high degree of immunity since the Salk vaccine program was launched in 1955, with the possibility of contracting the disease reduced on the average of 75% for fully vaccinated as compared with nonvaccinated persons.

The recommended basic schedule for all persons except young infants was three doses of 1 ml. each. The second injection would come four to six weeks after the first, the third, 7 to 12 months later, and the fourth a year or more later. For infants under 6 months of age a series of three injections of 1 ml. each, spaced one month apart and beginning as early as 2 months of age, and a fourth injection 7 to 12 months after the third was recommended.

Members of the advisory committee are Col. Donald M. Alderson, USAF (MC) assistant for professional services, Office of the Assistant Secretary of Defense (Health and Medical); Dr. Gordon Brown, professor of epidemiology, University of Michigan School of Public Health; Lieut. Col. Joseph W. Cooch, chief, Communicable Disease Branch, Department of the Army; Dr. Edward C. Curnen, chairman, Committee on the Control of Infectious Diseases, American Academy of Pediatrics; Dr. Geoffrey Edsall, chairman, Committee on Immunization of the Armed Forces Epidemiology Board, Walter Reed Hospital; Dr. Hollis S. Ingraham, first deputy commissioner, New York State Health Department; Dr. Cyrus Maxwell, Washington medical liaison, American Medical Association; Dr. Andrew C. Offutt, Indiana health commissioner, Dr. James C. Overall, president of the American Academy of Pediatrics; Dr. Julian P. Price, Chairman of the Poliomyelitis Committee of the American Medical Association; Dr. Thomas M. River, vice-president in charge of medical affairs, the National Foundation; Dr. Jonas Salk, professor of experimental medicine and director of virus research laboratory, School of Medicine, University of Pittsburgh; and a number of officials from the Public Health Service.

GOVERNMENT RENEWS STAND ON LIVE POLIOVIRUS VACCINE

Despite a generally optimistic survey of live poliovirus vaccines by a group of private scientists, the federal government served notice that it would turn down applications for licensing such a vaccine in the United States at this time.

U. S. Surgeon General Leroy E. Burney declared that on the basis of available scientific information the Public Health Service would not be carrying out its responsibility for insuring that a product is safe, potent, and capable of commercial production if it licensed the live vaccine now.

Instead, the official urged the nation to "go full speed ahead" in using the killed-virus vaccine developed by Dr. Jonas Salk. He called for a "door-to-door and face-to-face" campaign to vaccinate al who have not received the injections. Special emphasis should be placed on reaching the low socioeconomic groups, which contain the larg proportion of unvaccinated persons, he said.

(Continued on next page)

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Riseman, J. E. F., *et al.*: Circulation *17*:22, 1958

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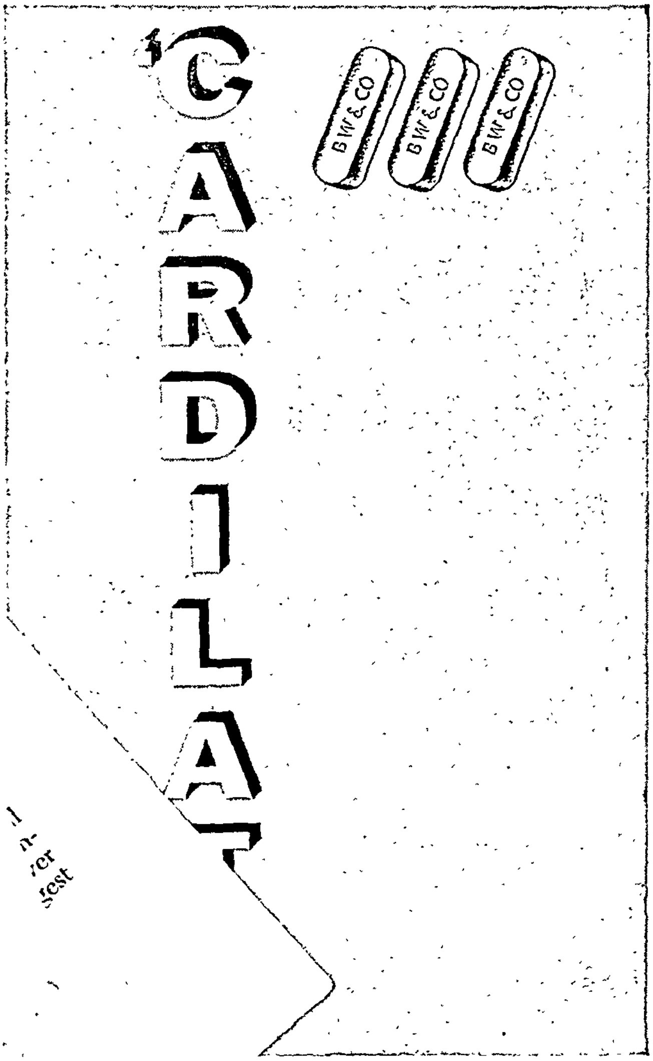


At a week's conference here sponsored by the World Health Organization and the Pan-American Health Organization, experts from 17 nations proclaimed the live virus vaccines safe, cheap, and effective. They recommended their use internationally, but at the same time proposed continued widespread use of Salk vaccine.

In backing the live virus vaccines, the scientists agreed in a summary statement that problems still remain. "It was recognized," the statement said, "that the use of a product that spreads beyond those originally vaccinated represents a radical departure from present practices in human preventive medicine."

Some of the scientists said there was a possibility that the living vaccine viruses might revert to dangerous strains that could cause an epidemic, although the general consensus was that this would not happen. So far no untoward results have been reported from the vaccinations of millions of persons abroad, including more than 1,000,000 in Russia, they pointed out.

Dr. Burney held that there was a need for more controlled studies of the live virus vaccine's use. Trials to date have taken place in countries where the children, "unlike those in the United States and in other more developed nations, normally develop immunity at an early age because of the widespread occurrence of the polio virus," he said.

PHS will follow present studies in the field with the hope that a safe live virus vaccine will be developed which could be taken orally and would thus be easier to administer, and which may provide longer-lasting immunity at lower costs, Dr. Burney told a news conference.

FLEMMING QUESTIONS INCREASE IN MEDICAL RESEARCH OUTLAYS

Arthur S. Flemming, Secretary of Health, Education, and Welfare, warned that if a Senate-passed increase in medical research funds becomes law, 5,000 to 6,000 scientific and medical personnel would have to be recruited for research work. He told a news conference that some of these undoubtedly would have to be "siphoned away" from teaching posts and private practice. If the additional money is to be used intelligently, Flemming said, then the extra personnel would be required.

The Senate approved 481 million dollars for the National Institutes of Health for the current fiscal year, 137 million dollars more than the House and 187 million dollars more than the administration requested.

The Senate also voted more money for Veterans Administration medical programs. Medical administration and miscellaneous operating expenses were increased by 4 million dollars over the House figure to a total of $31,349,000. Total appropriation for medical research in the VA under the Senate bill would be $19,300,000. The Senate increased by 3 million dollars the appropriation for construction of VA hospitals and domiciliary facilities, for a total of $33,100,000 more than the administration sought. The Senate went along with the House figure for inpatient care—792 million dollars, $5,300,000 more than the administration recommended. For outpatient care both houses provided $83,800,000, the administration figure.

A. M. A. BACKS AIR POLLUTION CONTROL MEASURE

The American Medical Association has supported legislation to extend the Air Pollution Control Act, under which the federal government helps states and localities to study ways of reducing harmful substances in the atmosphere.

"It is apparent that future research on the subject of air pollution and its relation to health is highly desirable," said Dr. F. J. L. Blasingame, A. M. A. Executive Vice-president, in a letter to Rep. Kenneth A. Roberts (D., Ala.), chairman of a House commerce subcommittee. "Although the interest of the federal government in the subject of air pollution may not be a permanent one, we feel that sufficient federal responsibility can still be demonstrated to justify the appropriation of limited federal funds in support of research activities in this field for an additional period of time," the A. M. A. official declared.

Dr. Blasingame noted that the philosophy of the act recognized the primary responsibility of state and local governments in controlling air pollution. The present law, authorizing 5 million dollars of federal aid annually, was scheduled to expire June 30, 1960, unless Congress took further action.

HEARINGS ON INTERNATIONAL MEDICAL RESEARCH BILL

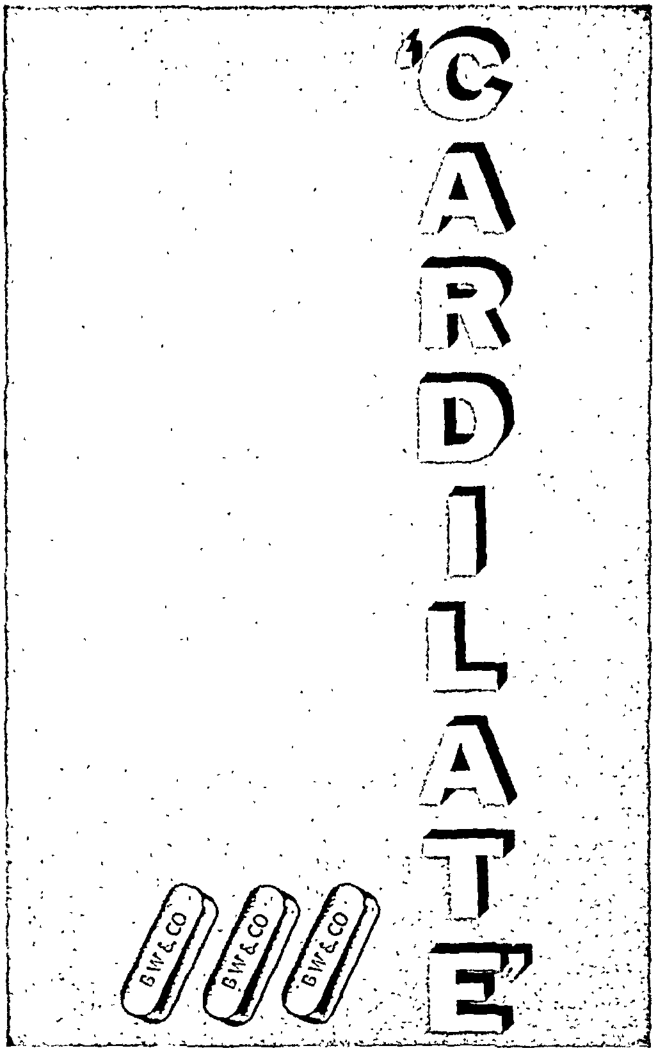
The Senate-passed measure authorizing a 50-million-dollar program for international medical research cooperation was slated for hearings July 21-23 before a House commerce subcommittee headed by Rep. Kenneth A. Roberts (D., Ala.). The bill, which would create a new National Institute for International Health and Medical Research, was overwhelmingly approved by the Senate earlier this session.

The administration opposed the bill as it stands and planned to urge the House to change it, including elimination of the flat 50-million-dollar annual authorization.

Meanwhile, a Senate government operations subcommittee called prominent physicians to testify July 9 and July 16 on the long-range trends, opportunities, and problems in international medical research. The subcommittee is headed by Sen. Hubert H. Humphrey (D., Minn.), who has traveled extensively abroad investigating medical research matters. Witnesses scheduled to testify included Dr. James Shannon, head of the National Institutes of Health; Dr. Paul Dudley White, heart specialist; Dr. Edward L. Bortz, geriatrics researcher; Dr. George N. Papanicolaou, cancer researcher; Dr. William G. Lennox, specialist in epilepsy; Dr. Clement Smith of Boston Lying-in Hospital; Dr. H. J. Muller of the University of Indiana; Dr. George Stevenson of the National Association for Mental Health; and Dr. Nicholson J. Eastman of Johns Hopkins University.

MISCELLANY

HEW Secretary Flemming urged food processors to submit requests to clear harmless chemical additives used in food with the Food and Drug Administration. He noted that only 26 requests have been submitted so far for the government clearance that is required under a recent law.



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MEETINGS

AMERICAN MEDICAL ASSOCIATION: Dr. F. J. L. Blasingame, 535 North Dearborn St., Chicago 10, Executive Vice-President.
1959 Clinical Meeting, Dallas, Texas, Dec. 1-4.
1960 Annual Meeting, Miami Beach, Fla., June 13-17.
1960 Clinical Meeting, Washington, D. C., Nov. 29-Dec. 2.
1961 Annual Meeting, New York City, June 26-30.
1961 Clinical Meeting, Denver, Nov. 28-Dec. 1.
1962 Annual Meeting, Chicago, June 13-17

AMERICAN

1959

July

American Society of Facial Plastic Surgery, New York City, July 17. Dr. Samuel M. Bloom, 123 E. 83rd St., New York 28, Secretary.

Oregon Cancer Conference, University of Oregon Medical School, Portland, July 16-17. Dr. Martin A. Howard, 1115 S. W. Taylor St., Portland 5, Ore., Chairman.

Rocky Mountain Cancer Conference, Brown Palace Hotel, Denver, July 22-23. Dr. N. Paul Isbell, 835 Republic Bldg., Denver 2, Chairman.

August

American Congress of Physical Medicine and Rehabilitation, Hotel Leamington, Minneapolis, Aug. 30-Sept. 4. Miss Dorothea C. Augustin, 30 N. Michigan Ave., Chicago 2, Executive Secretary.

American Dietetic Association, Statler Hilton, Los Angeles, Aug. 25-28. Miss Ruth M. Yakel, 620 N. Michigan Ave., Chicago 11, Executive Secretary.

American Hospital Association, Statler Hotel, New York City, Aug. 24-27. Dr. Edwin L. Crosby, 18 E. Division St., Chicago, Director and Secretary.

American Veterinary Medical Association, Hotel Muehlebach, Kansas City, Mo., Aug. 24-28. H. E. Kingman Jr., D.V.M., 600 S. Michigan Ave., Chicago 5, Executive Secretary.

Biological Photographic Association, Inc., Sheraton-Mount Royal Hotel, Montreal, Canada, Aug. 31-Sept. 3. Miss Jane H. Waters, Box 1668, Grand Central P. O., New York 17, Executive Secretary.

National Medical Association, Detroit, Aug. 10-13. Dr. John T. Givens, 1108 Church St., Norfolk, Va., Secretary.

Nevada State Medical Association, Reno, Aug. 19-22. Dr. Gilbert G. Lenz, 505 S. Arlington Ave., Reno, Nev., Chairman.

Northwest Proctologic Society, Timberline Lodge, Mount Hood, Ore., Aug. 26-29. Dr. John L. McKay, 645 Medical Dental Bldg., Seattle 1, Secretary-Treasurer.

Rocky Mountain Radiological Society, Shirley-Savoy Hotel, Denver, Aug. 20-22. Dr. John H. Freed, 4200 E. Ninth Ave., Denver 20, Secretary-Treasurer.

Society for Clinical and Experimental Hypnosis, Fairmont Hotel, San Francisco, Aug. 3-5. Dr. Irving Schwartz, 2340 Sutter St., San Francisco 15, Chairman, Program Committee.

Southeastern Oklahoma Clinical Symposium, McAlester Clinic, McAlester, Aug. 8-9. Mr. Charles A. Miller, McAlester Clinic, McAlester, Okla., Business Manager.

West Virginia State Medical Association, The Greenbrier, White Sulphur Springs, Aug. 20-22. Mr. Charles Lively, P. O. Box 1031, Charleston 24, Executive Secretary.

September

American Association of Medical Clinics, Sheraton-Blackstone Hotel, Chicago, Sept. 24-26. Dr. Edwin P. Jordan, Box 58, Charlottesville, Va., Executive Secretary.

American Association of Obstetricians and Gynecologists, The Homestead, Hot Springs, Va., Sept. 10-12. Dr. E. Stewart Taylor, 4200 E. Ninth Ave., Denver 20, Secretary.

American Association for the Surgery of Trauma, Mount Washington Hotel, Bretton Woods, N. H., Sept. 24-26. Dr. William T. Fitts Jr., 3400 Spruce St., Philadelphia 4, Secretary.

American College of Gastroenterology, Biltmore Hotel, Los Angeles, Sept. 19-26. Mr. Daniel Weiss, 33 W. 60th St., New York 23, N. Y., Executive Director.

American College of Surgeons, The Traymore Hotel, Atlantic City, N. J., Sept. 28-Oct. 2. Dr. Paul R. Hawley, 40 E. Erie St., Chicago 11, Director.

American College of Surgeons, Ohio Chapter, Statler Hotel, Cleveland, Sept. 11-12. Dr. Berton M. Bogle, 311 S. Market, Troy, Ohio, Secretary-Treasurer.

American Roentgen Ray Society, The Netherland Hilton Hotel, Cincinnati, Sept. 22-25. Dr. C. Allen Good, Mayo Clinic, Rochester, Minn., Secretary.

American Society of Clinical Pathologists, The Palmer House, Chicago, Sept. 7-11. Mr. Claude E. Wells, 2052 N. Orleans, Chicago 14, Executive Secretary.

Central Association of Obstetricians and Gynecologists, Drake Hotel, Chicago, Sept. 24-26. Dr. Edwin J. DeCosta, 104 S. Michigan Ave., Chicago 3, Secretary.

College of American Pathologists, The Palmer House, Chicago, Sept. 6. Dr. Arthur H. Dearing, Suite 2115, Prudential Plaza, Chicago 1, Executive Director.

Colorado State Medical Society, Brown Palace and Shirley Savoy Hotels, Denver, Sept. 8-11. Mr. Harvey T. Sethman, 835 Republic Bldg., Denver 2, Executive Secretary.

International College of Surgeons, Tennessee Section, Chattanooga, Sept. 28-29. Dr. William G. Stephenson, Medical Arts Bldg., Chattanooga, Tenn., Regent.

Kentucky State Medical Association, Columbia Auditorium, Louisville, Sept. 22-24. Mr. Joseph P. Sanford, 1169 Eastern Pkwy., Louisville 17, Ky., Executive Secretary.

Maryland, Medical and Chirurgical Faculty of the State of, Semiannual Meeting, Ocean City, Sept. 18. Mr. John Sargeant, 1211 Cathedral St., Baltimore 1, Executive Secretary.

Medical Progress Assembly, Tutwiler Hotel, Birmingham, Ala., Sept. 13-15. Dr. Herbert H. Thomas, 920 S. 19th St., Birmingham, Ala., Chairman, Publicity Committee.

Michigan State Medical Society, Pantlind Hotel, Grand Rapids, Sept. 28-29, Oct. 1-3. Mr. William J. Burns, 606 Townsend St., Lansing 15, Mich., Executive Secretary.

Mid-Continent Psychiatric Association, Holiday Inn Motor Hotel, St. Louis County, Mo., Sept. 18-20. Dr. W. Payton Kolb, Baptist Medical Arts Bldg., Little Rock, Ark., Secretary.

Montana Medical Association, Finlen Hotel, Butte, Sept. 17-19. Mr. L. Russell Hegland, 1236 N. 28th St., Billings, Mont., Executive Secretary.

National Recreation Congress, Morrison Hotel, Chicago, Sept. 28-Oct. 2. Mr. Jesse Reynolds, Department of Recreation and Parks, The Mosque, Laurel and Main Streets, Richmond 20, Va., Chairman.

North American Federation, International College of Surgeons, Chicago, Sept. 13-17. For information write the Secretariat, 1516 Lake Shore Dr., Chicago 10.

Oregon State Medical Society, Medford Hotel, Medford, Sept. 23-25. Mr. Roscoe K. Miller, 1115 S. W. Taylor St., Portland 5, Ore., Executive Secretary.

Tennessee Valley Medical Assembly, Chattanooga, Tenn., Sept. 28-29. Dr. Guy M. Francis, 109 Medical Arts Bldg., Chattanooga 2, Tenn., Chairman.

United States Section, International College of Surgeons, Palmer House, Chicago, Sept. 13-17. Dr. Ross T. McIntyre, 1516 Lake Shore Dr., Chicago 10, Executive Secretary.

Utah State Medical Association, Hotel Utah Motor Lodge, Salt Lake City, Sept. 16-18. Mr. Harold Bowman, 42 S. 5th East, Salt Lake City 2, Executive Secretary.

Washington State Medical Association, Olympic Hotel, Seattle, Sept. 13-16. Mr. Ralph W. Neill, 1309 Seventh Ave., Seattle 1, Executive Secretary.

World Medical Association, Montreal, Canada, Sept. 7-12. Dr. Louis H. Bauer, 10 Columbus Circle, New York 19, Secretary-General.

October

Academy of Psychosomatic Medicine, Sheraton-Cleveland Hotel, Cleveland, Oct. 15-17. For information write: Dr. Bertram B. Moss, Suite 1035, 55 E. Washington St., Chicago 2, Secretary.

American Academy of Ophthalmology and Otolaryngology, The Palmer House, Chicago, Oct. 11-16. Dr. William L. Benedict, 15 Second St., S. W., Rochester, Minn., Executive Secretary.

American Academy of Pediatrics, The Palmer House, Chicago, Oct. 5-8. Dr. E. H. Christopherson, 1801 Hinman Ave., Evanston, Ill., Executive Secretary.

American Association of Medical Assistants, Benjamin Franklin Hotel, Philadelphia, Oct. 16-18. Mrs. Stella Thurnau, 510 N. Dearborn, Room 924, Chicago 10, Executive Secretary.

American Association of Medical Record Librarians, Radisson Hotel, Minneapolis, Oct. 12-15. Miss Margaret G. Scully, 510 N. Dearborn St., Chicago 10, Director.

American College of Cardiology, Benjamin Franklin Hotel, Philadelphia, Oct. 23-25. Dr. Philip Reichert, Empire State Bldg., New York 1, Executive Director.

American College of Chest Physicians, 25th Anniversary Homecoming Meeting, Albuquerque, N. M., Oct. 14-17. Mr. Murray Kornfeld, 112 E. Chestnut St., Chicago 11, Executive Director.

American College of Preventive Medicine, Hotel Ambassador, Atlantic City, N. J., Oct. 21-22. Dr. John J. Wright, P. O. Box 1267, Chapel Hill, N. C., Secretary-Treasurer.

American Heart Association, Trade and Convention Center, Philadelphia, Oct. 23-27. Mr. William F. McGlone, 44 E. 23rd St., New York 10, Secretary.

American Medical Writers' Association, Chase Hotel, St. Louis, Oct. 2-3. Dr. Harold Swanberg, 510 Maine St., Quincy, Ill., Secretary.

American Otorhinologic Society for Plastic Surgery, Inc., Conrad Hilton Hotel, Chicago, Oct. 11. Dr. Joseph G. Gilbert, 75 Barberry Lane, Roslyn Heights, N. Y., Secretary.

American Psychiatric Association, Detroit Divisional Meeting, Hotel Statler, Detroit, Oct. 29-31. Dr. Benjamin Jeffries, 16321 Mack Ave., Detroit 24, Co-Chairman, Planning Committee.

American Public Health Association, Convention Hall, Atlantic City, N. J., Oct. 19-23. Dr. Berwyn F. Mattison, 1790 Broadway, New York 19, N. Y., Executive Director.

American School Health Association, Claridge Hotel, Atlantic City, N. J., Oct. 18-23. Dr. A. O. DeWeese, 515 E. Main St., Kent, Ohio, Executive Secretary.

American Society of Anesthesiologists, Inc., Americana Hotel, Bal Harbor, Fla., Oct. 5-9. Mr. John W. Andes, 188 W. Randolph St., Room 1101, Chicago 1, Executive Secretary.

American Society of Facial Plastic Surgery, Chicago, Oct. 15-17. Dr. Samuel M. Bloom, 123 E. 83rd St., New York 28, Secretary.

American Society of Plastic and Reconstructive Surgery, Hotel Fountainebleau, Miami Beach, Fla., Oct. 18-23. Dr. Thomas Ray Broadbent, 508 E. South Temple, Salt Lake City, General Secretary.

American Society of Tropical Medicine and Hygiene, Claypool Hotel, Indianapolis, Oct. 28-31. Dr. Rolla B. Hill, 3575 St. Gaudens Road, Miami 33, Fla., Executive Secretary.

Association of Clinical Scientists, Sheraton-Park Hotel, Washington, D. C., Oct. 10. Dr. Robert P. MacFate, 323 Northwood Rd., Riverside, Ill., Secretary-Treasurer.

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CORTICOSTEROID THERAPY IN RHEUMATOID ARTHRITIS

COMPARATIVE STUDY OF EFFECTS OF PREDNISONE AND PREDNISOLONE, METHYLPREDNISOLONE, TRIAMCINOLONE, AND DEXAMETHASONE

David H. Neustadt, M.D., Louisville, Ky.

Lack of documented comparative information has led to increasing confusion regarding relative merits of the various corticosteroid preparations in treatment of rheumatoid arthritis. Tested in a group of 65 patients with active rheumatoid arthritis were prednisone, prednisolone, methylprednisolone, triamcinolone, and dexamethasone. Comparable antirheumatic benefit was obtained with all compounds in the majority of patients. No one preparation demonstrated any consistently superior therapeutic advantage. Factors influencing choice of treatment include probable effectiveness, nature of unwanted side-effects, ease of administration, and cost to the patient.

ALMOST daily an avalanche of "drug literature" promoting one of the various available corticosteroid preparations pours into the offices of the majority of practicing physicians. Each piece of "literature" is cleverly prepared to call attention to an "improved product" which will provide optimum benefit and/or will cause less toxic side-effects when used in a wide variety of systemic disorders, including rheumatoid arthritis.

A lack of documented comparative information in the literature has led to increasing confusion regarding the relative merits, special properties, and tendency to unwanted effects of the various preparations (prednisone, prednisolone, methylprednisolone, triamcinolone, and dexamethasone) in the treatment of rheumatoid arthritis.

There is general agreement among most investigators who have had experience with corticosteroids in rheumatoid arthritis that this form of therapy, when properly administered, is clinically useful in patients with active rheumatoid arthritis in whom the usual measures have failed to adequately control the disease. The majority of clinical studies to date indicate that the initial synthetic analogues, prednisone and prednisolone, are superior to both cortisone and hydrocortisone in treating rheumatoid arthritis.[1] Their significant therapeutic advantage is not the greater antirheumatic potency, as manifested by the reduced dosage on a weight basis (milligram for milligram), but the reduced tendency to provoke sodium and fluid retention and potassium loss when these compounds are given in therapeutic dosage.

From the Arthritis Clinic and Department of Medicine, School of Medicine, University of Louisville.

Recently three additional synthetic analogues[2] have been made available for use in rheumatoid arthritis. Now when it is considered necessary to add a corticosteroid to the regimen of a patient with rheumatoid arthritis, the physician is offered the choice of five different synthetic compounds.

The decision as to which of these five corticosteroids should be selected must obviously be based on the relative merits and hazards of each preparation. The specific factors to be considered include (1) clinical effectiveness; (2) severity, nature, and incidence of unwanted side-effects; (3) ease of administration and dosage schedule; and (4) cost to patient.

It was hoped that by obtaining comparative data with the above considerations in mind the information derived might help answer the following practical questions: 1. Which of the available steroid agents is the best or at least most suitable for use in a patient with rheumatoid arthritis? 2. Is any one of the agents more useful for certain special features of the disease? 3. What are the maximum, minimum, and optimum dosage levels of each agent? 4. Are there any special criteria one can use as a guide in selecting one agent in preference to the others? 5. Can certain precautions be safely relaxed with one or more of the compounds? 6. Is there actual evidence of a reduced tendency to adverse effects from any of the current preparations? 7. What are the effects of the various drugs on associated disorders, such as diabetes, peptic ulcer?

Table 1.—*Composition of Series (Sixty-five Patients)*

Sex of Patients		Age Distribution, Yr.	
Males	26 (40%)	Average age	54.6
Females	39 (60%)	Range	23-71
Duration of Arthritis, Yr.		Stage of Disease*	
1-5	30 (46%)	1	9 (14%)
5-10	19 (29%)	2	25 (38%)
10-21	16 (25%)	3	17 (26%)
Average duration	7 yr.	4	14 (22%)

* According to the criteria of the American Rheumatism Association, Steinbrocker and others.[5]

Rationale of Procedure

There is no completely reliable plan or method of evaluating a new agent in rheumatoid arthritis that is not associated with certain shortcomings. To control all variables that come into play in a chronic disease of unknown origin subject to spontaneous fluctuations is a problem which has recently received well-deserved attention.[3]

Short-term observations may be misleading. However, if one omits patients from a study who received a drug for short periods, one may be accused of influencing the final statistical results. Also there may have been some important reason for withdrawing the drug early in the study.

Double-blind and random selection studies are considered by some to disclose results of greater scientific precision than the older and more conventional type of evaluation study. However a double-blind technique also carries with it certain disadvantages that may compromise its value. In conducting studies with a relatively inactive drug (slowly acting agent), such as an antimalarial agent or a gold salt, a double-blind study can be carried out.[4] When employing a corticosteroid which has powerful suppressive capacity, abrupt withdrawal and placebo substitution is immediately noticed by the majority of patients. Sudden discontinuance also is not without danger because of the possibility of producing a marked degree of adrenal insufficiency. This hypoadrenal state can become an acute and serious medical emergency. Also random selection introduces a number of patients who may be unreliable and are not suitable for testing. Thus, it is almost impossible to carry out such a program without both influencing patients and introducing added difficulties.

For these reasons patients were carefully screened to include only those with well-established rheumatoid arthritis of over one year's duration and to exclude hyperreactors, unreliable patients, and hypersensitive ones.

Material and Methods

Composition of Series.—Observations are derived from 65 patients with definite active rheumatoid arthritis. The composition of the series as to sex, age distribution, duration of disease, and stage is given in table 1. There were 39 females and 26 males. The ages of the 65 patients ranged from 23 to 71 years. The average duration of the disease was 7 years, varying from 1 year to 21 years. Each patient was classified as to stage of severity and functional class according to the criteria established by the American Rheumatism Association.[5] Thirty-one patients (48%) were in stages 3 and 4 (moderately advanced and advanced).

None of the patients had received antimalarial agents or gold therapy within one year of the initiation of corticosteroids. Basic management programs, including the use of salicylates and/or other simple analgesics in regular and adequate dosage, regulated rest, and the use of various thermal agents and supervised exercises, had been instituted in all patients.

Methods of Evaluation.—All patients had been observed for reasonable control periods prior to receiving any special therapy. To determine clinical effects, an evaluation of each patient was performed at regular and frequent intervals. Objective assessment was based on the therapeutic criteria devised by the American Rheumatism Association.[5] Measurement of swollen joints, changes in surface temperature and skin color over inflamed joints, and estimation of ranges of motion of involved joints were recorded at each appraisal. Whenever possible, subcutaneous rheumatoid nodules were measured and their consistency was estimated. Radiographs of selected joints were repeated when indicated. Temperature, pulse, weight, and blood pressure were recorded at each examination.

Certain laboratory studies were performed on each patient periodically. These included (1) hemoglobin level and hematocrit, (2) white blood cell count and differential cell count, (3) erythrocyte sedimentation rate, (4) total plasma protein and albumin-globulin fractions, and (5) urinalysis for sugar and albumin. Blood glucose determinations were performed irregularly but whenever considered indicated. Serum sodium and potassium levels were determined on several separate occasions on each patient.

Upper gastrointestinal x-ray studies were done before therapy in every patient with any history of symptoms suggestive of a possible gastrointestinal disorder. In those patients who developed any gastrointestinal symptoms during the administration of steroids, radiographic examination was made of the gastrointestinal tract.

Method of Administration.—All corticosteroid agents used in the study were supplied as oral preparations in the form of tablets containing exclusively the biologically active substance. Forty-eight patients received prednisone and/or prednisolone for an average duration of two years. (Many patients received these agents for periods of over three years.) These patients constituted the basic group from which comparison data on prednisone and prednisolone were derived. Since previous studies [6] had demonstrated no significant difference in the clinical and metabolic effects of prednisone and prednisolone given at the same dosage level, to simplify their presentation in the final analysis these two agents are reported as a single drug (prednisteroids). Methylprednisolone was administered to 39 patients. Of this group 32 had received long-term prednisteroids, 25 had received triamcinolone either before or after methylprednisolone, and 7 patients received this analogue as sole steroid medication. Triamcinolone was given to a total of 38 patients. Thirty-one of these patients had received prednisteroids, 25 had received either maintenance doses of methylprednisolone or were changed to this analogue after trial with triamcinolone, and in 7 patients this was the only form of steroid treatment.

The total daily dosage was divided routinely into four doses, given at five-hour to six-hour intervals around the clock, usually ingested near meal times and at bedtime. Adjustments in dosage were made by small increments or decrements of 1 or 2 mg. at intervals of 5 to 10 days in accord with the response of the patient. The maintenance dosage was considered the smallest amount of the drug that would satisfactorily control the symptoms of the disease and keep the patients ambulatory and active. After a well-established maintenance dosage had been achieved, patients were transferred to another analogue at the same dosage level. Since the size, shape, and color of the different tablets were not always uniform, patients were simply told that it was the same medicine in a different form. Placebo substitution during prednisone, prednisolone, and triamcinolone treatment periods was carried out early in the study, but after and during administration of methylprednisolone and dexamethasone, patients served as their own controls without placebo interruption. Medication was never changed from one analogue to another until a relatively stable maintenance dosage was reached.

All patients were managed on an ambulatory basis, with the exception of short periods of hospitalization for some patients who developed complications or needed special studies.

Basic treatments were administered concurrently. Intra-articular therapy was given to isolated troublesome joints at intervals in some patients. An attempt was made to compare the frequency of the need of this procedure during treatment with the various agents. No special diet or supplements were prescribed, unless found indicated.

Late in the study, dexamethasone, a newer steroid agent not commercially available at the time, was administered to 40 patients for periods up to six months and results are included to allow preliminary comparisons of response, side-effects, and dosage requirements.

Clinical and Laboratory Results

Clinical.—A total of 25 patients received prednisone or prednisolone, methylprednisolone, and triamcinolone on separate occasions for periods of sufficient duration to allow satisfactory comparative analysis. Appraisal of therapeutic response was not attempted in the 40 patients who did not receive a trial with each corticosteroid preparation under study. Data compiled on these patients are included chiefly for purposes of statistical evaluation of unwanted effects and dosage requirements.

Although spontaneous fluctuations in the activity of the disease required temporary changes in dosage, a similar degree of clinical improvement could be obtained with all preparations in the majority of patients. The dosage required to sustain this equivalent control varied from time to time, from patient to patient, and even in the same individual from time to time. For instance, one patient who was under adequate control, on a "stable" maintenance dose of 12 mg. of methylprednisolone, required 14 mg. of triamcinolone for similar control, and when shifted back to methylprednisolone then needed 15 mg. to regain equivalent control. In some patients therapeutic response was definitely improved when shifted from one analogue to another at the same dosage level, but this was not a consistent finding. In changing patients from prednisone or prednisolone to triamcinolone, although the arthritis objectively was as good or even improved, some patients described a "let down" or a feeling of increased fatigue. This reaction also occurred in some patients changed to methylprednisolone, but to a lesser degree.

Although some patients derived enhanced benefit from one steroid compared with another, the chief differences were improvement or retrogression of a subjective nature. Striking rapid suppressive effect was obtained with all steroids in the majority of patients who received this form of treatment for the first time. In the majority of those patients who were changed from one to another at the same dosage level, no immediate objective improvement occurred. This was expected since most of these patients were at an optimal or suboptimal level when treatment was initiated.

Therapeutic grade response varied considerably,[5] and although a slightly greater number of patients obtained grade 1 or 2 responses with methylprednisolone and triamcinolone, it was felt that this upgrading could have been achieved by increasing doses of prednisolone, if undesirable effects had not interfered.

TABLE 2.—*Comparative Summary of Side-effects in Twenty-five Patients on Therapy with Four Corticosteroids*

Side-effects	Predni-steroids	Methylpred-nisolone	Triam-cinolone
Moon facies	16	9	7
Hirsutism	5	8	6
Acne	2	1	0
Anorexia	0	0	4
Emotional disturbances, mild	1	1	1
Headaches and/or dizziness	1	2	3
Hot flashes and/or erythema	0	2	4
Muscle weakness	0	0	5
Ecchymosis and/or purpura	4	7	6
Elevated blood pressure	1	0	1
Glycosuria	4	1	0
Gastrointestinal symptoms (negative x-ray)	9	2	6
Peptic ulcer	2	1	1[*]
Weight loss, marked	0	0	8
Masking of infection	0	1	0
Osteoporosis with compression fracture	0	0	0
Phlebitis	1	0	0

[*] Gastric hemorrhage, ulcer not demonstrated.

No significant change in functional class was noted when strict adherence to criteria was used, in spite of some patients' comments of improvement during administration of newer analogues.

The average duration of prednisteroid treatment was 23.2 months, ranging from 6 to 40 months; the average duration of methylprednisolone treatment was 8 months, ranging from 4 to 14 months; the average duration of triamcinolone therapy was 8½ months, ranging from 4 to 16 months.

Thus in the majority of patients, the antirheumatic effect of all steroids used was satisfactory. Superior anti-inflammatory properties were not evident when dosage was adjusted, except when increased dosage had been limited by side-effects.

Adequate suppression of disease activity was accomplished with prednisolone in doses of less than 20 mg. in the majority of patients. The daily dose ranged from 5 to 20 mg. and the average maintenance total daily dose was 11.4 mg. In 31 patients who were transferred from prednisolone to triamcinolone, the average maintenance dose was reduced to 7.8 mg. without sacrificing any of the benefits obtained and ranged from 2 to 16 mg. In 32 patients changed to methylprednisolone, the average maintenance dosage was 8.12 mg., ranging from 4 to 15 mg. The average maintenance dose of methylprednisolone needed for comparable clinical benefit in patients was essentially the same as that of triamcinolone.

Laboratory.—No consistent significant laboratory alterations were noted which could be definitely attributed to any of the drugs in this study. Sedimentation rates decreased to normal or near normal levels in some patients, usually paralleling an improved clinical state. Hemoglobin level and hematocrit also seemed uninfluenced by any steroid medication, and when improvement occurred in these blood indexes it seemed to be associated with an improved clinical state. Glycosuria occurred more frequently with prednisolone and prednisone than with methylprednisolone or triamcinolone. Blood sugar levels increased in several patients during prednisone and prednisolone treatment and rarely during methylprednisolone and triamcinolone therapy, but the increase was neither pronounced nor consistent. Serum sodium and potassium determinations were essentially unchanged during treatment with all preparations.

Undesirable Effects

The side-effects that occurred during therapy in the 25 patients who received all four preparations—prednisteroids, methylprednisolone, and triamcinolone—are listed for comparison in table 2.

Nearly all patients who received prednisone and/or prednisolone displayed some manifestation of hypercortisonism. "Mooning" with fat pads occurred more frequently during prednisolone therapy than during methylprednisolone or triamcinolone treatment periods. Transient glycosuria also was found more often during prednisolone therapy. Edema occurred in a significantly higher incidence with prednisolone and cleared in most cases when the patient was changed to either methylprednisolone or triamcinolone. Certain side-effects such as hot flashes, erythema of face, and excessive perspiration occurred almost exclusively during triamcinolone therapy. These were of an annoying nature in some patients, but usually could be tolerated. The most important untoward effect during triamcinolone administration was pronounced weight loss which was not always accompanied by anorexia. In five of eight patients there was a concomitant loss of muscle tissue associated with extreme weakness. In this group of patients peptic ulcer was discovered in two patients during prednisolone therapy and in one patient during methylprednisolone therapy. One patient suffered a gastric hemorrhage while receiving triamcinolone. The incidence of peptic ulcer disease was low considering the fact that these 25 patients had received steroid treatment over protracted periods.

Nine patients (36%) receiving prednisone developed gastrointestinal symptoms with normal gastrointestinal x-ray studies, as compared to six patients (24%) receiving triamcinolone and two patients (4%) receiving methylprednisolone. No patient in this group incurred a spontaneous fracture secondary to steroid osteoporosis. Cutaneous purpuric and ecchymotic manifestations occurred in a slightly higher frequency during methylprednisolone therapy.

In table 3 is listed the over-all frequency of side-effects that occurred during administration of prednisolone, methylprednisolone, and triamcinolone in the 65 patients.

Moon facies occurred in over 50% of patients receiving all hormones. This feature was slightly more frequent with prednisone (60%) and was least frequent with triamcinolone (50%).

Evidence of fluid retention as manifested by edema was found commonly during prednisolone administration (29% of patients) but was unusual with both methylprednisolone and triamcinolone. Edema cleared in all but two patients receiving methylprednisolone and persisted in only one patient during triamcinolone treatment.

Disturbance in carbohydrate metabolism occurred in six patients or 12½% of the patients receiving prednisolone, in two patients or 5% of the group on methylprednisolone therapy, and in only one patient or 2½% of those receiving triamcinolone.

Nonspecific gastrointestinal symptoms without demonstrable organic cause developed in 16 patients or 33% of the 48 patients receiving prednisolone, in 10 patients or 25.6% of 39 patients during methylprednisolone therapy, and in 12 patients or 31.5% of 38 patients under triamcinolone treatment. In the majority of these patients the addition of an antacid controlled the symptoms so that therapy could be continued.

"New" peptic ulcer was found in a total of six patients. This over-all incidence of 9% was equally divided between prednisolone, methylprednisolone, and triamcinolone, with two instances each. One patient, cited earlier in this paper, in the course of receiving triamcinolone in a total daily dose of 5 mg., suffered a severe gastric hemorrhage. She was also taking large amounts of salicylates daily. No evidence of ulceration was discovered by radiologic examination of the gastrointestinal tract; nevertheless, this complication is listed as a side-effect resulting from triamcinolone. Some patients who were known to have peptic ulcers before treatment periods were given methylprednisolone and/or triamcinolone. The precaution of administering a strict ulcer regimen was taken in these patients. No complications or recurrences of ulceration occurred.

Emotional disturbances of a troublesome nature were observed in 4 of the 48 patients receiving prednisolone, in 1 of the 39 patients receiving methylprednisolone, and in 2 of the 38 patients receiving triamcinolone.

Ecchymotic and purpuric skin manifestations occurred in 14 instances or in 35.8% of patients receiving methylprednisolone. These cutaneous side-effects were found in only 14% of patients during prednisolone therapy and in 23% of the triamcinolone group.

Of noteworthy interest are certain untoward effects which appear to be chiefly confined to triamcinolone. The most important of these was characterized by considerable weight loss accompanied in some patients with pronounced weakness and noticeable loss of subcutaneous and muscle tissue.[7] This occurred in nine patients to some degree and was sufficiently marked in three patients to necessitate withdrawal of triamcinolone. When these patients were transferred to methylprednisolone or prednisolone, weight returned to or toward normal levels and "weakness" with loss of muscle strength gradually subsided. In only five patients was anorexia extremely marked. In some patients who had significant weight loss, depression of appetite did not occur. The average weight loss of the entire group on triamcinolone therapy was 6.8 lb. (3.1 kg.). In 10 patients weight loss ranged from 5 to 10 lb. (2.3 to 4.5 kg.); in 3 patients over 10 lb. was lost and in 2 of these weight loss was 22.5 and 23.5 lb. (10.2 and 10.6 kg.) respectively. It was not possible to predict in which patients this phenomenon would occur; in patients who were overweight, in whom some weight loss would have been welcomed, weight was maintained.

Certain other side-effects, such as hot flashes, erythema of face and neck, and increased perspiration which have been previously described as common accompaniments of triamcinolone therapy[2c] occurred with greater frequency, but although they

TABLE 3.—*Summary of Side-effects in Sixty-five Patients on Therapy with Four Corticosteroids*

Side-effects	Predni-steroids (48 Patients)	Methylprednisolone (39 Patients)	Triamcinolone (38 Patients)
Moon facies	29 (60%)	22 (56%)	19 (50%)
Hirsutism	9	8	9
Acne	4	4	2
Anorexia, marked	0	0	5
Emotional disturbances	4 (8%)	1	1
Weakness	1	0	9 (23.6%)*
Elevated blood pressure	3	0	1
Edema	14 (29%)	2	1
Glycosuria	6 (12.5%)	2	1
Gastrointestinal symptoms (negative x-ray)	16 (33%)	10 (25.6%)	12 (31.5%)
Peptic ulcer	2	2	8†
Weight loss, marked	0	0	10
Ecchymosis and/or purpura	7 (14%)	14 (35.8%)	9 (23.6%)
Masking of infection	1	1	0
Osteoporosis with fracture	1	0	0
Phlebitis	1	0	0
Peripheral neuritis	1	1	1

* Required discontinuance of therapy in three patients.

† Includes one instance of gastric hemorrhage without evidence of ulcer.

were annoying to some most patients tolerated these symptoms with minimal complaints. Of interest is the fact that these "vasomotor phenomena" did not occur with regularity in the patients who developed marked anorexia, muscle weakness, and/or weight loss.

Dexamethasone

Dexamethasone, the newest analogue,[2d] only recently made available commercially, has been administered to 40 patients with active rheumatoid arthritis, for periods up to six months.

Observation periods are too short from which to draw definite conclusions but long enough to suggest trends of responsiveness, information as to dosage requirements, and early tendency to unwanted effects. The average maintenance dose of dexamethasone required to obtain antirheumatic clinical control similar to that of the older steroids was 1.4 mg. daily. Maintenance doses ranged from 0.75 mg. to 2.75 mg. It is available in either a scored 0.5-mg. or 0.75-mg. size tablet so that adjustments had to be made in increments and decrements of 0.25 mg. If a smaller size tablet had been available, it is possible that some patients would have been controlled on an even smaller dosage.

Dexamethasone is obviously an extremely powerful anti-inflammatory agent, on a milligram for milligram potency basis, when compared with the other widely used compounds. However, the criterion for an improved product is not dosage or potency but rather a reduced incidence of undesirable side-effects. To date, no serious complications have occurred. However, the periods of observation are too short to evaluate this most important phase of the drug's properties. It is noteworthy that the agent has shown a marked propensity to increase appetite to an excessive state and that a concomitant weight gain has been found in a majority of the patients. The average weight gain for all patients was 10.25 lb. (4.6 kg.). In 7 patients weight gain ranged from 0.5 to 5 lb. (0.23 to 2.3 kg.); in 9 patients 5 to 10 lb. (2.3 to 4.5 kg.); in 14 patients 10 to 15 lb. (4.5 to 6.8 kg.); in 6 patients 15 to 20 lb. (6.8 to 9.1 kg.); and in 1 patient it exceeded 20 lb. In only two patients was there no weight disturbance. In several patients this troublesome effect reached disturbing levels and it was necessary to withdraw the drug to halt this "unhealthy" weight increase. Whereas weight gain occurred without evidence of discernible edema in most instances, a peculiar unilateral (dependent) edema occurred in several patients. The possibility of the existence of a local lymphatic or vascular disturbance was always considered, but definite evidence of such a disorder was lacking and response to usual measures was poor. This curious finding occurred in five patients. Abatement of the painless edema occurred when these patients were changed to another analogue.

Symptoms such as increased fatigue, loss of pep, weakness, sleepiness, and insomnia also were described. There seemed to be a reduction in the occurrence of cutaneous ecchymotic and purpuric lesions. Further study is necessary with this promising new steroid.

Comment

Although refinements through modifications of the steroid nucleus have accomplished "improved" and impressive preparations in certain aspects, the results are obviously not wholly confined to the plus side of the ledger. Indeed each "contender" for the prize of "best steroid" in the "rheumatoid arthritis class" has shown great power and speed, but alas each has also shown the tendency to "hit below the belt" at times, and not infrequently when least expected. Each of the new analogues has displayed enhanced antirheumatoid potency as compared to the older steroids. Using the data from the patients in the present study as well as those of other workers, the rank in antirheumatoid potency shows dexamethasone the most potent (average total daily dose 1.4 mg.), triamcinolone and methylprednisolone next with triamcinolone a fraction more potent (average total maintenance dose 7.8 mg. and 8 mg., respectively), and prednisone and prednisolone the least potent on a weight basis (average total daily dose 11.4 mg.). Although this difference is of obvious interest it has little practical significance since equivalent antirheumatoid potency can be obtained by simply increasing the dosage of the less potent agents. And since adequate clinical control of rheumatoid arthritis can be obtained by employing any one of the agents in usual therapeutic dosage, a more powerful agent is rarely needed.

Hence, our chief attention must be directed to the untoward effects of the drugs. With prednisolone as the "standard" by virtue of the greater experience with this agent, its side-effects and those of methylprednisolone and triamcinolone were compared. Prednisolone has shown less tendency to produce electrolyte disturbances, especially sodium retention and subsequent fluid accumulation, when compared with its antecedents, cortisone and hydrocortisone.

Methylprednisolone has shown even less tendency to cause edema. Disturbances of carbohydrate metabolism and untoward effects on the gastrointestinal tract were significantly reduced compared with prednisolone. Other unwanted effects were comparable to those resulting from prednisone and prednisolone, but a definite trend to lessening of certain of these effects was noted. No new adverse side-effects were evident. A higher incidence of cutaneous purpura could possibly be attributed to methylprednisolone.

Triamcinolone, on the other hand, seemed to "create" some troubles not usually encountered in the use of either prednisolone, hydrocortisone, or cortisone. Two groups of "new" undesirable effects were found. One was of a minor but annoying nature, the other a potentially serious complication. The first group included symptoms that were manifest chiefly in the skin such as hot flashes, erythema of face and neck, and increased perspiration. Although these symptoms are nonspecific and were occasionally described by patients receiving other steroids, they occurred with sufficient regularity, subsided when patients were transferred to other steroids, and returned when triamcinolone therapy was resumed in a large enough percentage of those receiving the agent to reasonably conclude that there was a probable cause-and-effect relationship. The possibility of chance association would seem remote.

The other set of unwanted effects was characterized by marked weight loss associated with weakness and in some of the more severe cases actual muscle wasting.[7a] Anorexia was present in some, but not all, of these patients. Initial weight loss in some patients was considered evidence of a diuretic effect with sodium excretion and a loss of hidden edema fluid, but this explanation could not account for continued weight loss and shrinkage of muscle tissue. In three patients, in whom arthritis was under excellent control, the weakness was so severe that it was disabling. The cause of this unusual phenomenon is obscure. It would seem to be a selective overactive catabolic action with probable excessive nitrogen excretion. It has been suggested that associated with the negative nitrogen balance there is a strong potassium losing effect not reflected in serum potassium levels.[8] This would explain, partly at least, the severe weakness. High-protein diets, protein supplements, and mixed hormones did not alter this picture. No special increase in osteoporosis was disclosed in comparative skeletal roentgenograms of these individuals nor did any suffer compression fractures.

The likelihood of turning this troublesome effect of triamcinolone to an advantage in overweight patients was explored. Unfortunately depression of appetite did not occur with any uniform success in these individuals. Some patients who developed excessive appetites and marked weight gains during dexamethasone therapy were given half of their steroid requirement in triamcinolone and the other half in dexamethasone in an effort to curb appetite and weight gain. A favorable effect was seen in only one of five patients so treated. It was not possible to predict in advance which patients would be susceptible to continued weight loss and weakness. Usually, however, this effect was present early, but in two instances significant weakness and weight loss did not begin until after three and four months, respectively, of drug administration. The influence of size of dose was not considered significant.

It would be unfair to attempt any final comparison of the incidence and frequency of side-effects resulting from dexamethasone with those from the other steroids. But, although its use has been limited with regard to time, some comment is deserved in connection with its tendency for causing excessive appetite and marked weight gain. Whereas the majority of patients "leveled off" after the initial gain, a significant number gained excess weight, and in several the drug had to be withdrawn after every attempt to hold weight gain had been exhausted. This newest agent, although powerful, is obviously not without its faults.

The infrequency of occurrence of emotional disturbances with the newer corticoids is noteworthy. Significant mental symptoms were not observed in patients during methylprednisolone, triamcinolone, and dexamethasone therapy. Prednisone and/or prednisolone produced a stimulating effect manifested by mild euphoria in some patients, similar to that not infrequently encountered during cortisone and hydrocortisone therapy. Although in some patients this effect was considered helpful, its abolition in the newer compounds is not a significant disadvantage, since the patients who acquired this false elation were often those subject to mood swings, depressions, and other serious emotional disturbances, sometimes difficult to control.

When employed skillfully with due respect for potency and potential side-effects of these agents, any one of them might serve satisfactorily. Only trial and careful observations will enable the clinician to determine which preparation will be the most useful in an individual patient. Occasionally one of the corticosteroids may show greater therapeutic advantage than the others in an individual patient.

All corticosteroids require careful regulation of dosage as well as close observation of the patients for side-effects. Dosage must be determined in accord with the response of the patient. No arbitrary limits can be set as to minimum dosage. Although side-effects occurred in patients receiving small doses, it is reasonable to assume that the smaller the dose, the greater the safety factor.

No "best" prize can be awarded at this writing. It would appear from these comparative observations that methylprednisolone probably is the steroid of choice for initial trial in a patient with rheumatoid arthritis. It is potent and displays a slightly improved "safety" record, showing a reduced frequency of disturbing side-effects as compared with the other steroids.

Although further experience will be needed to determine the relative place of dexamethasone with regard to side-effects, certainly its remarkable effect on appetite and associated weight gain must be given serious study. This effect, sometimes helpful initially in the underweight or thin patient with acute rheumatoid arthritis, can become troublesome later. The combination of dexamethasone and triamcinolone has not so far been rewarding enough to recommend it as other than an experiment under certain special circumstances.

Summary

Observations were carried out on the effects of prednisone and/or prednisolone, methylprednisolone, triamcinolone, and dexamethasone in a series of 65 patients with active rheumatoid arthritis.

Twenty-five of these patients received each agent under study on separate occasions for periods of sufficient duration to warrant comparative analysis. Forty of the patients did not receive a trial with each preparation and data compiled from this group are included for purposes of evaluation of undesirable effects and dosage requirements. Clinical trials with dexamethasone were carried out in 40 patients for periods up to six months to allow preliminary assessment of therapeutic response, side-effects, and dosage schedules.

Comparable antirheumatic benefit was obtained with all compounds under study in the majority of patients. Appreciable differences in therapeutic benefit were noted in some patients, but no preparation demonstrated consistent superior therapeutic advantage.

On a weight basis, milligram per milligram, dexamethasone was the most potent steroid, with an average maintenance dose of 1.4 mg. The average maintenance dose of methylprednisolone was essentially the same as that of triamcinolone. Prednisone and prednisolone were the least potent, with an average maintenance dose of 11.4 mg.

The factor that chiefly limits the value of prolonged steroid therapy in rheumatoid arthritis is the frequency and severity of undesirable side-effects. The incidence of minor physiological effects of hypercortisonism (moon facies, hirsutism, acne) was comparable in all the corticoids under study. The occurrence of peptic ulcer and gastrointestinal symptoms without evidence of ulceration was similar with all compounds. Emotional disturbances, glycosuria, and edema occurred in a significantly higher incidence during prednisone and prednisolone administration. Ecchymosis and/or purpura was observed in 36% of patients receiving methylprednisolone, 23.6% of patients receiving triamcinolone, and in only 14% of patients receiving prednisolone therapy. No "new" adverse reactions resulted from use of methylprednisolone. Certain undesirable features, including hot flashes, erythema of the face, and increased perspiration, were found almost exclusively during triamcinolone therapy. However, the major untoward effect attributed to this hormone was muscle weakness, sometimes associated with marked weight loss. These side-effects resulting from triamcinolone usually subsided after patients were transferred to another steroid. Preliminary observations suggest that the frequency of side-effects occurring during dexamethasone administration is similar to that of the older steroids. Dexamethasone has a remarkable appetite-stimulating effect. Excessive appetite associated with striking weight gain occurred in the majority of patients.

A combination of two different steroidal agents (dexamethasone and triamcinolone) was employed in a small number of patients without significant success.

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The triamcinolone used in this study was supplied as Aristocort through Dr. Christopher H. Demos by Lederle Laboratories Division, American Cyanamid Company, Pearl River, N. Y.; the methylprednisolone was supplied as Medrol through Dr. Hubert C. Peltier by the Upjohn Company, Kalamazoo, Mich.; and the dexamethasone was supplied as Decadron through Dr. Nicholas E. Capeci by Merck Sharp & Dohme, West Point, Pa.

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CIRCULATING LIPIDS IN DIABETES MELLITUS

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Many patients with diabetes mellitus present abnormalities in levels of circulating lipids in absence of ketoacidosis and renal disease. These are characterized by elevation of serum fatty acid and triglyceride levels, with only moderate or no increase of serum cholesterol and phospholipid levels. Two factors are involved; they are decompensation of deranged carbohydrate metabolism (lack of insulin) and presence of vascular complications. If maintenance of normal levels of circulating lipids is added to the criteria of management in diabetes mellitus, prognosis for such patients may be improved, especially in regard to complications. Findings are based on data obtained in clinical studies of 94 patients with diabetes compared with similar studies of 24 normal healthy persons.

Disturbances in lipid metabolism are an essential part of the deranged metabolism in diabetes mellitus.[1] In the preinsulin era, diabetic ketosis and acidosis, the severest manifestations of disturbed lipid metabolism, were the cause of death of many patients with diabetes mellitus. At present, abnormalities of lipid metabolism rarely produce these dramatic consequences but are probably responsible for the high incidence of vascular disease among diabetics.[2]

Our own studies have been concerned with circulating lipids in diabetes.[3] Extremely high serum lipid levels have been observed occasionally in patients with diabetes mellitus in absence of ketonuria. The highest figure was 16 Gm. of total lipid per 100 ml. of serum, seen in a patient with the syndrome of diabetes mellitus and idiopathic hyperlipemia.[3a] The serum of patients with this disorder is milky or creamy in the fasting state. Marked elevation of serum triglycerides and total lipids is associated with a less pronounced increase of serum cholesterol and phospholipid. The disturbance in carbohydrate metabolism encountered in this group is usually mild. Good control can usually be achieved by diet regulation without the use of insulin or orally given substitutes. There is a remarkable correlation between serum lipid levels and blood sugar levels. Adequate control of disturbed carbohydrate metabolism produces marked reduction of all serum lipid levels. Contrariwise, inadequate diabetes control (hyperglycemia) is associated with a superimposed elevation of serum triglyceride and often also of serum cholesterol and phospholipid levels. During these periods of exacerbation in both carbohydrate and lipid metabolism, eruptive xanthoma of the skin and lipemia retinalis may be seen.

It was thought that the abnormal changes in blood sugar and serum lipid levels in patients with both metabolic disorders represent rather rare extremes and that milder disturbances of a similar nature may occur perhaps more often in patients with diabetes.[4] Observations in patients with early diabetic retinopathy without evidence of renal disease and without ketonuria presenting increased levels of serum triglycerides and total lipids, despite normal serum cholesterol and phospholipid levels, supported this concept.[3b] Perhaps too little emphasis has been placed, as in atherosclerosis research, on serum lipid fractions other than cholesterol.[5]

Selection of Patients

It appeared profitable, therefore, to study 94 especially selected patients with diabetes for simultaneous disturbances in the metabolism of carbohydrates, lipids, and lipoproteins.

The patients of this sample, 43 men and 51 women, were selected on the basis of age and onset of diabetes. The ages of the groups averaged 55 to 63 years, and the onset of diabetes was about uniformly at middle age. They had been under medical observation for periods varying from 6 months to 12 years (average, 4.2 years). They were divided into four groups. Patients in groups 1 and 2 were chosen because of absence of clinical, electrocardiographic, or roentgenographic evidences of cardiovascular, peripheral vascular, or renal disease. In contrast, each patient in groups 3 and 4 had either coronary artery or peripheral vascular disease but no evidence of nephropathy. The diabetes of patients in groups 1 and 3 was well controlled, with average fasting blood sugar levels of 114 and 101 mg.% respectively; none had a level above 150 mg.%. The diabetes of patients in groups 2 and 4 was inadequately controlled, with

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average fasting blood sugar levels of 193 and 198 mg.% respectively; none had a level lower than 150 mg.%. Acetonuria was uniformly absent in all patients during the study.

There was a preponderance of women except in group 3. Group 1 consisted of 23 women and 21 men, group 2, 16 women and 9 men, group 3, 4 women and 7 men, and group 4, 8 women and 6 men. Of the 44 patients in group 1, 15 were treated with insulin, 9 with tolbutamide, and 20 by dietary regulation solely. Of the 25 patients of group 2, 14 were treated with insulin, 8 with tolbutamide, and 3 by diet alone. Of the 11 patients of group 3, 4 were treated with insulin, 3 with tolbutamide, and 4 by diet alone. Of the 14 patients of group 4, 12 were treated with insulin, 2 with tolbutamide, and none by diet alone.

The control group consisted of 24 apparently healthy persons, 14 women and 10 men, with an average age of 57 years, who presented no clinical or laboratory evidences of diabetes or cardiovascular disease. They were examined with the other patients during the period of this study.

TABLE 1.—*Laboratory Data on Ninety-four Patients with Diabetes and Twenty-four Controls*

Group*	Av. Age, Yr.	Fasting Blood Sugar, Mg. %	Total Cholesterol, Mg. %	Cholesterol Ester, Mg. %	Phospholipid, Mg. %	Total Lipid, Mg. %	Total Fatty Acid, mEq./Liter	Fatty Acids, mEq./Liter		
								Cholesterol Esters	Phospholipid	Triglycerides
Control (24 patients)	57	...	248	184	290	851	13.0	4.8	6.7	1.7
	± 6.8	...	± 22.7	± 16.7	± 36.0	± 98.8	± 1.81	±0.45	±0.91	±1.55
1 (44 patients)	58	114	272	203	294	924†	14.5	5.3	6.8	2.6
	±12.1	± 20.1	± 43.3	± 31.4	± 45.5	±138	± 3.19	±0.81	±1.06	±2.04
2 (25 patients)	55	193	262	195	288	972‡	16.9	5.1	6.7	5.2
	±13.7	± 28.7	± 60.7	± 44.8	± 48.0	±239	± 5.32	±1.17	±1.09	±3.75
3 (11 patients)	63	101	283	208	292	937	15.0	5.4	6.8	2.8
	±10.1	± 24.7	± 54.1	± 37.6	± 53.7	±238	± 4.40	±0.97	±1.24	±2.87
4 (14 patients)	61	198	308	225	339	1,113§	21.9	5.8	7.9	8.2
	± 8.0	± 32.0	± 47.8	± 39.7	± 43.6	±163	± 4.30	±1.03	±1.01	±4.13

* 1, no complications, FBS <150, Mg. %; 2, no complications, FBS >150, Mg. %; 3, vascular complications, FBS <150, Mg. %; 4, vascular complications, FBS >150 Mg. %.
† Based on 42 determinations.
‡ Based on 24 determinations.
§ Based on 12 determinations.

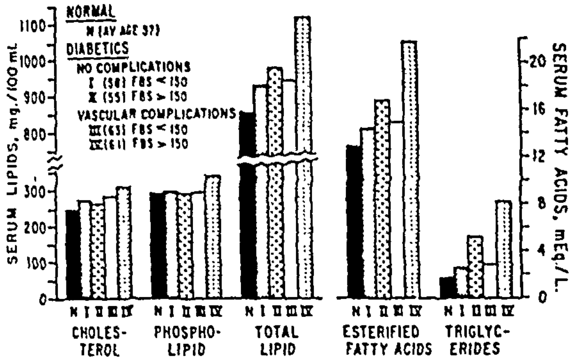
Procedure and Methods

Venous blood was drawn in the morning, after a fast of at least 12 hours, for simultaneous determinations of blood sugar, serum lipid, and lipoprotein levels. This was done between 9 and 10 a. m. The blood sugar level was determined by the Folin-Wu method, the serum total and esterified cholesterol levels by the method of Schonheimer and Sperry, the phospholipid level by the Sperry modification of the Subbarrow method, the total lipid level by the Bloor method, and the fatty acids level by the Stern and Shapiro method in the Tompsett and Tennant modification.[6] The serum triglyceride level was calculated by subtracting from the fatty acids the sum of fatty acids combined in the esterified cholesterol and the phospholipids.[1d] Serum lipoprotein levels were determined by paper electrophoresis with use of the method of separation, staining, and estimation previously described from this laboratory.[7] The blood sugar level was determined immediately after the blood was drawn, and the serum lipids were extracted, as a rule, on the same day. Only occasionally was the serum preserved at 4 C for one to two days. Extensive experience in our laboratory indicates that under these circumstances no changes in the concentrations of the individual lipid fractions occur.

Results

The control group showed circulating lipid levels which may be considered normal for the average age of 57 years (table 1). A comparison of this group with the four groups of patients with diabetes reveals the following differences: Patients without vascular complications and with a normal blood sugar level (group 1) differed from the nondiabetic controls only by a moderate, probably nonsignificant, elevation of serum fatty acid, triglyceride, and total lipid levels; the levels of serum cholesterol and phospholipid did not differ from those of the controls. It is of interest that diabetics without manifest vascular complications but with elevated blood sugar levels (group 2) exhibited decided increases in serum fatty acid, triglyceride, and total lipid levels, with normal levels of serum cholesterol and phospholipid. This is important because the patients of this group differed from those in group 1 only in one respect, i. e., the decided elevation of blood sugar level, indicating inadequate compensation of the error in carbohydrate metabolism.

The findings in diabetics with vascular complications (groups 3 and 4) are even more interesting, although the numbers of patients in these groups were small (11 and 14). Those patients with normal blood sugar levels (group 3) did not differ essentially from diabetics with normoglycemia without vascular manifestations (group 1). In contrast, those with vascular complications and hyperglycemia (group 4) presented the severest abnormalities of circulating lipids seen in this study. With only a moderate elevation of serum cholesterol and phospholipid levels, there was a striking increase in the serum fatty acid level by approximately 80% and triglyceride level by over 400%, with a decided increase in total lipids. It is of interest that adequate *compensation of the deranged carbohydrate* metabolism in patients with vascular complications but without manifest renal involvement resulted in a marked reduction of circulating lipids toward normal levels. The differences between the four groups are depicted in the figure. It may be seen that the differences within the four groups of patients with diabetes consisted mainly in serum fatty acids, triglycerides, and total lipids and to a much lesser degree in cholesterol and phospholipid.



Graphic presentation of changes in levels of circulating lipids in four groups of diabetics and control group of similar average age. In contrast to slight elevation of serum cholesterol and phospholipid levels in group 4, there is decided elevation of levels of serum fatty acids, triglycerides, and total lipids, especially in groups 2 and 4. FBS=fasting blood sugar level above or below 150 mg.%.

Table 2 presents the average values of α, β, and 0 lipoprotein fractions. A significant change in the electrophoretic pattern is seen in group 4. It consisted of a decrease of the α-lipoprotein fraction from 28.0 to 21.6% with a corresponding increase in the 0 fraction from 23.6 to 29.8%. The differences between the other groups are less significant. The 0 fraction is closely related to the low density lipoproteins, chylomicrons, and serum triglycerides.

Comment

Studies of lipid metabolism in diabetes may be divided into two groups. One group of workers has concentrated on circulating lipids, especially cholesterol and lipoproteins; recently, nonesterified fatty acids, important in the transport and perhaps mobilization of lipids, have received increasing attention.[1] Another group has been concerned with oxidation and synthesis of fatty acids in tissues of diabetic animals.[8] In diabetes, probably because of lack of insulin, there appears to be a block in the synthesis of long-chain fatty acids at the 4-carbon stage. The possibility that additional blocks in lipogenesis are involved is not excluded. Deposition and mobilization of fatty acids in fat tissue, especially under the influence of insulin, has received increasing attention.[9]

In studying circulating lipids in patients with diabetes, those in ketoacidosis must be separated from those without. Circulating lipid levels are decidedly elevated in ketoacidosis, and adequate compensation of the deranged carbohydrate metabolism with insulin reverses these changes to normal. Serum fatty acid and triglyceride levels show the earliest and most pronounced elevation, whereas cholesterol and phospholipid levels are less affected.[10]

It is important that diabetics, in the absence of ketoacidosis, may present well-characterized abnormalities in circulating lipids. These changes are related to two factors: (1) compensation of the deranged carbohydrate metabolism (lack of insulin) and (2) presence of vascular complications.

The importance of the first factor is drastically demonstrated in patients presenting the syndrome of diabetes and idiopathic hyperlipemia.[3a] Decompensation of carbohydrate metabolism, manifested by hyperglycemia and glycosuria, is associated with pronounced additional elevations of serum fatty acid and triglyceride levels, even in absence of ketonuria. Control of hyperglycemia results invariably in reduction of these serum lipid fractions to lower levels.

Other patients with diabetes, without idiopathic hyperlipemia, exhibit elevations of the identical serum lipid fractions in varying degrees. In a previous study, a group of patients with diabetes under good control and without any manifest complications exhibited slight increases of neutral fats and total lipids; another group with early retinopathy exhibited significant elevations of these serum lipid fractions without any changes in serum cholesterol and phospholipid; patients with advanced nephropathy had the severest abnormalities which involved all circulating lipid fractions.[3b]

Table 2.—*Average Serum Lipoprotein Levels in Ninety-four Patients with Diabetes*

Group	No. of Patients	Total Stainable Lipid, %		
		Alpha	Beta	0
1	44	28.0 ± 7.46	48.4 ± 9.10	23.6 ± 8.38
2	25	28.4 ±10.0	46.6 ± 8.75	25.0 ± 8.06
3	11*	24.7 ± 6.81	50.6 ± 9.93	24.7 ±10.3
4	14	21.6 ± 6.8	48.6 ± 8.33	29.8 ± 8.27

*Based on 10 determinations.

The present study confirms and expands these observations on a larger scale. Patients with nephropathy, ketosis, and acidosis were a priori excluded, and, for purposes of comparison, a control group without diabetes and clinical vascular disease and of the same average age was included. Diabetics whose carbohydrate metabolism was adequately compensated by insulin, tolbutamide, or diet alone and who had no evidences of vascular disease showed a mild elevation of serum fatty acids and triglyceride levels. In a second group of patients, without vascular disease but with inadequate compensation of carbohydrate metabolism, decided increases in levels of the above-mentioned serum lipid fractions were noted and again in presence of normal levels of serum cholesterol and phospholipid. Thus, even in diabetics with adequate control by the present standards, a mild abnormality in circulating lipids was seen which was enhanced by inadequate compensation of the defect in carbohydrate metabolism. In children with diabetes the relations between serum lipids and lipoproteins and blood sugar levels are perhaps more pronounced than in adults.[11]

The importance of the second factor, vascular complications, was illustrated in the other groups. Patients with vascular complications but adequate compensation of deranged carbohydrate metabolism did not differ significantly in regard to the circulating lipids from those without vascular complications, whereas those with inadequate compensation presented the severest abnormalities of the entire sample, with almost double levels of serum fatty acids and fourfold levels of serum triglycerides. It is important then that, even in presence of overt vascular complications, adequate control of carbohydrate metabolism may mitigate the derangement in circulating lipids in diabetes. It may be repeated, however, that none of the patients of this study had symptoms or signs of the Kimmelstiel-Wilson syndrome or other evidences of overt renal disease with the associated abnormalities in circulating lipids.

Our observations support the concept of a disorder of lipid metabolism in patients with diabetes mellitus. Whether this is an independent disturbance or a faulty correlation of carbohydrate and lipid metabolism, perhaps traceable to the tissues (adipose tissue), cannot be decided. On the basis of clinical and experimental work, disturbances of lipid metabolism in diabetes mellitus may be classed in three categories: (1) increased lipolysis from the depots, liberating neutral fats and triglycerides; (2) disturbed storage of lipid in tissues, resulting in delayed clearance of circulating neutral fats and triglycerides; and (3) impaired synthesis or esterification of fatty acids. Definite correlation of the abnormalities in circulating lipids in a given case of diabetes with one or more of these categories is at present impossible. They appear to be related to the disordered carbohydrate metabolism and lack of insulin.

The maintenance of normal levels of circulating lipids, especially of fatty acids and triglycerides, should be added to the criteria of management of diabetes, especially in patients with vascular complications. Normal levels of these compounds will reflect normal transport and synthesis of lipids.

The main problem in the management of diabetes mellitus as we see it today is prevention of vascular disease. Whether strict maintenance of this new parameter of diabetes control will improve the prognosis of patients with diabetes, especially in regard to vascular complications, remains to be investigated.

Summary

Many patients with diabetes mellitus present well-characterized abnormalities in levels of circulating lipids in absence of ketoacidosis and renal disease. These are characterized by elevation of the levels of serum fatty acids and triglycerides with only moderate or no increase in the levels of serum cholesterol and phospholipid. They are mainly related to two factors: (1) decompensation of deranged carbohydrate metabolism (lack of insulin) and (2) presence of vascular complications. Maintenance of normal levels of circulating lipids should be added to the criteria of management of diabetes mellitus. Observation of this parameter of diabetes control may improve the prognosis of patients with diabetes, especially in regard to the complications. Adequate compensation of deranged carbohydrate metabolism appears to be an important prerequisite for adequate control of lipid metabolism.

Fifth Ave. and 100th St. (29) (Dr. Adlersberg).

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A NEW, POTENT ANTIHYPERTENSIVE DRUG

PRELIMINARY STUDY OF [2-(OCTAHYDRO-1-AZOCINYL)-ETHYL]-GUANIDINE SULFATE (GUANETHIDINE)

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The antihypertensive effects of orally given guanethidine have been studied in 18 patients hospitalized for hypertensive cardiovascular disease. In seven of these, therapy with either reserpine or chlorothiazide or both was continued during the administration of guanethidine. Amounts of guanethidine needed to maintain a satisfactory blood pressure under these conditions ranged from 25 mg. every other day to 150 mg. thrice daily. These dosage levels caused bradycardia in nine patients and transient, mild diarrhea in eight. Orthostatic hypotension occurred in all patients; in two the blood pressure in the supine position was not reduced. Laboratory tests showed that injections of guanethidine modified the responses of experimental animals to subsequent injections of either pressor or depressor drugs.

Antihypertensive drugs with different chemical structures and modes of action are always of great interest to physicians treating hypertensive patients. The compounds recently synthesized by Mull and his associates,[1] i. e., [2-(octahydro-1-azocinyl)-ethyl]-guanidine sulfate (Su 5864) and hexahydro-1-azepinepropionamidoxime dihydrochloride (Su 4029) for these reasons are of special interest. The former has been given the generic name guanethidine by the manufacturer. The two substances differ importantly in that guanethidine contains an eight-membered instead of a seven-membered ring and a terminal guanidyl instead of an amidoxime group.

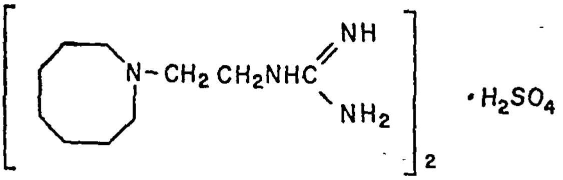

Fig. 1.—Structure of guanethidine.

Both substances have been shown to be antihypertensive when given intravenously in doses of 15 to 30 mg. per kilogram of body weight to dogs with experimental hypertension, but they did not affect the blood pressure of normal dogs.[2] The hypertension elicited by high doses of amphetamine or ephedrine was eliminated and the carotid occlusion reflex blocked. We have studied both substances, but especially guanethidine, in normotensive and hypertensive dogs and in hypertensive patients.

From the Research Division, the Cleveland Clinic Foundation, and the Frank E. Bunts Educational Institute.

Clinical Investigation

The antihypertensive effects of orally given guanethidine have been studied in 18 patients who received the drug daily for periods ranging from 2 to 12 weeks. All patients remained in hospital for evaluation of the severity of hypertensive cardiovascular disease and during the first two to four weeks of drug treatment. The conditions of nine of these had been observed for months or years during use of other antihypertensive regimens, and in seven therapy with either reserpine or chlorothiazide or both was continued during administration of guanethidine.

Table 1.—*Severity of Hypertensive Vascular Disease and Antipressor Responses in Patients Treated with Guanethidine*

				Severity Index									Av. Weekly Blood Pressure					
				Components									Control		1st Wk.		Last Wk.	
Case No.	Sex	Age, Yr.	Diagnosis	B.P.	Cardiac	Renal	Cerebral	Total	Previous Therapy	Concurrent Therapy	Weeks of Guanethidine Therapy	Dosage, Mg./Day	L[‡]	S	L	S	L	S
1	M	39	M.H.,[*] reversed	3	2	2.5	1.5	9.0	C,H,D[†]	D	10	450	182/129	146/113	197/137	139/108	194/131	135/96
2	M	49	E.H.	3	1	.5	1.5	6.0	D	...	9	100	199/137	186/139	178/120	146/116	166/108	102/77
3	M	52	E.H.	3	2	0	1.0	6.0	D	...	10	100	201/127	191/133	192/119	144/103	178/102	129/85
4	M	49	M.H., reversed	2	2	1.0	2.0	6.0	C,R,D	R,D	7	75	208/124	137/96	185/111	116/83	163/100	130/85
5	F	67	M.H., reversed	3	2	2.5	3.0	8.5	R,D	R,D	7	12.5	226/126	173/100	212/104	149/95	240/110	120/80
6	M	42	E.H.	2	4	2.0	1.5	8.5	...	...	6	150	178/125	168/125	157/118	156/122	173/86	127/73
7	M	41	E.H.	2	1	3.0	1.5	7.5	...	...	5	150	188/120	186/130	156/101	188/104	156/97	154/101
8	F	38	Pyelo.	1	0	3.5	1.0	5.5	...	...	6	75	186/110	158/105	183/112	149/99	164/98	130/90
9	F	58	Amyloid.	1	0	3.5	1.0	5.5	...	...	7	100	187/100	150/98	164/88	140/83	143/82	107/64
10	F	43	M.H.	2	1	3.0	2.0	8.0	C,R,D	C,R,D	2	200	215/108	161/96	175/104	131/86	174/102	134/79
11	M	53	M.H., reversed	2	2	1.5	1.5	7.0	M,D	...	4	200	207/113	199/118	186/102	155/94	166/91	137/80
12	M	56	E.H.	2	1	0	1.0	4.0	...	...	4	300	192/122	188/122	181/112	174/111	173/103	138/87
13	F	56	RAD	1	1	0	1.0	3.0	...	...	3	25	171/106	150/107	160/98	141/97	141/83	105/70
14	F	72	RAD	1	3	0	1.5	5.5	...	...	3	50	192/110	182/103	191/99	150/95	178/89	123/75
15	F	32	Sclero.	3	3	0	3.0	9.0	R,D	D	2	75	195/140	185/136	163/116	147/113	151/98	137/83
16	M	39	M.H., reversed	4	2	2.5	1.0	9.5	C,R,H,D	R	2	500	217/146	165/126	200/136	135/99	200/136	135/99
17	M	59	M.H., reversed	1	2	.5	1.0	4.5	R,D	R	2	100	208/108	193/105	187/102	169/97	174/96	156/81
18	M	49	E.H.	2	3	2.0	1.5	8.5	R	R	2	300	201/121	194/126	208/121	194/126	187/114	160/111

[*] M.H., reversed: malignant hypertension, reversed by treatment. E.H.: essential hypertension. Pyelo.: pyelonephritis. Amyloid: renal amyloidosis. M.H.: malignant hypertension. RAD: occlusive renal artery disease. Sclero.: scleroderma.

[†] C: chlorisondamine. H: hydralazine. D: chlorothiazide. R: reserpine. M: mecamylamine.

[‡] L: supine B.P. S: standing B.P.

[§] Office reading.

Table 2.—*Effects of Intermittent Therapy with Guanethidine on Supine Arterial Pressure*

Wk. of Observation	Av. Supine B. P.	Standing B. P.	Dosage, Mg./Day
1	201/127	191/133	...
2	192/119	144/103	150
3	191/112	112/79	...
4	184/109	138/91	50
5	185/109	122/85	...
6	195/116	147/101	...
7	193/113	151/104	100
8	182/107	122/84	200
9	178/108	129/85	200

The condition of the patient prior to use of this drug is summarized through the use of a numerical severity index.[3] This index allots 4 possible units to each of four areas of examination (diastolic blood pressure, functional cardiac capacity, and renal and cerebral statuses). The sum of the grades is called the total severity index (TSI); thus a patient with minimal hypertension and no signs of vascular disease would have a TSI of 1, and a patient with maximum hypertensive disease (diastolic average more than 140 mm. Hg, severe cardiac and renal failure, grade 4 hypertensive retinopathy, and hypertensive encephalopathy) would have a TSI of 16. These data for the 18 patients are recorded in table 1.

Brachial arterial pressure was measured four times daily with the patients in supine and standing positions while in the hospital and at home after discharge. Measurements were made weekly of urine protein excretion, hemoglobin level, and total and differential white blood cell counts. In the first three patients treated, sulfobromophthalein tests were performed.

Of the 18 patients treated, 16 had decreases in both supine and standing blood pressure, while in 2 only standing blood pressure was reduced. Orthostatic hypotension was severe in some patients, but it tended to become less severe or more tolerable except in two, in whom dosage reduction was necessary. In none of the patients has tolerance to the antihypertensive effects of the drug developed. Responses to the drug occurred in those patients with renal hypertension as well as in those with essential hypertension.

Decreases in arterial pressure were noted within four hours of the initial dose, but in some patients the antihypertensive effects were delayed for a week or more. The duration of action of the drug is prolonged, as illustrated by results in the patient who received intermittent treatment (table 2). Amounts of guanethidine required to maintain satisfactory reduction in blood pressure have ranged from 25 mg. every other day to 150 mg. three times daily. The initial daily dose used has ranged from 25 to 100 mg.

Diarrhea, an annoying but not serious side-effect, developed in eight patients and was partially controlled by atropine, 0.4 mg. four times daily. Bradycardia was noted in nine patients; in two of these it was unaffected by 0.4 mg. of atropine intravenously, but when the amount was increased to 0.8 mg. in one patient the pulse rate rose from 52 to 72 beats per minute.

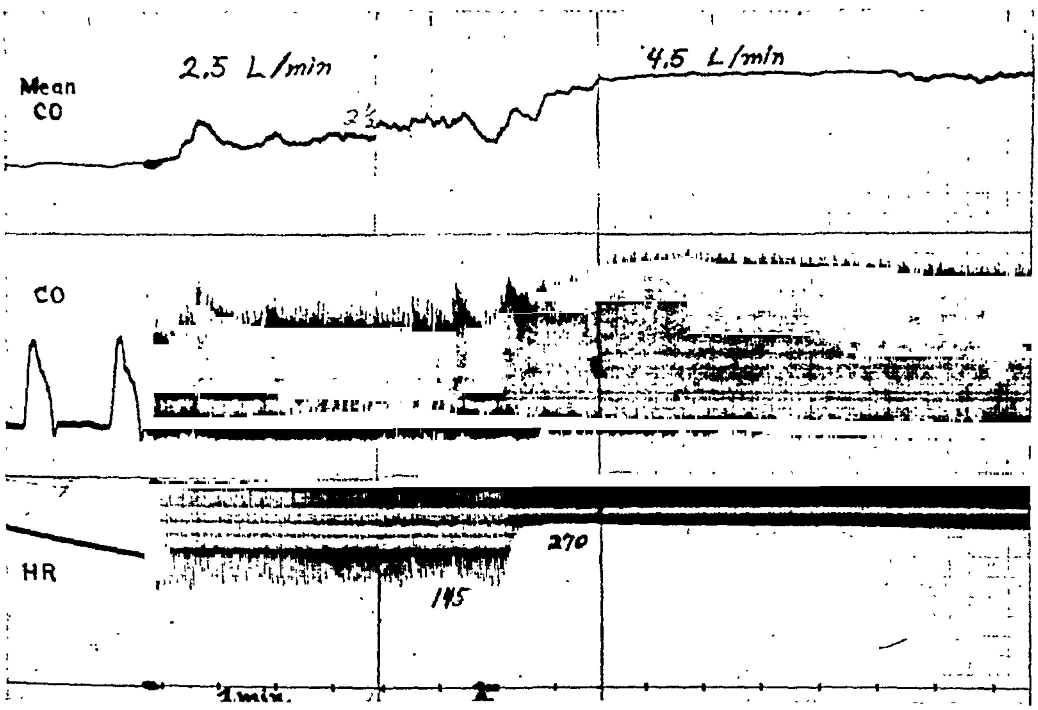

Fig. 2.—*Top line,* mean cardiac output. *Middle,* phasic cardiac output. Height of recording indicates peak ejection velocity of left ventricle. *Bottom recording,* heart rate. Length of lines is inversely proportional to rate. Injection of guanethidine, 15 mg. per kilogram of body weight, at (1). Time marker, one minute. Cardiac output increased 80%; heart rate increased 83%.

There was no evidence of toxic action of this drug as measured by hemoglobin level, blood cell count, urine protein excretion, or sulfobromophthalein excretion. Two patients have shown slight dependent edema, for which we have so far not accounted.

Su 4029 was studied in eight hypertensive patients. Significant decreases in supine arterial pressure occurred in only two of the eight patients, and in these fever developed. Diffuse myalgia occurred in one, necessitating discontinuance of use of the drug. Six patients had significant postural hypotension.

Pharmacological Studies

Effect on Arterial Blood Pressure in Anesthetized and Normal Dogs.—Doses of 10 to 15 mg. of guanethidine per kilogram were given intravenously to dogs under pentobarbital anesthesia and to unanesthetized ones. The arterial pressure fell sharply 40 to 50 mm. Hg and shortly thereafter rose 30 mm. Hg or more above the control levels. It might stay there for an hour or more, only slowly returning to the original level. During the course of a six-hour experiment without anesthesia, no fall in average blood pressure level occurred. Nor was it reduced the next day.

During the injection of guanethidine the animal immediately became quiet, lost interest in its environment, appeared apprehensive, vigorously licked its chops, and became tremulous. It was content to lie quietly until the stage of increased respiratory rate and fall in blood pressure was well over; then the normal ebullience slowly reappeared. The ocular light and touch reflex was not abolished during this period.

Effect on Aortic Flow (Cardiac Output).—The aortic flow, which is approximately equivalent to cardiac output, was measured by an electromagnetic flowmeter designed by Mr. F. Olmsted. Aortic flow is continuously measured by this method in unanesthetized, unrestrained dogs. An example of the effect of 15 mg. of guanethidine per kilogram is given in figure 2.

The marked increase in cardiac output is clearly evident, rising from 2.5 liters per minute to 4.0. The heart rate rose from 145 beats per minute to 270. For the period of 15 minutes that output was recorded, it remained at the high level.

TABLE 3.—*Examples of Effect of Intravenously Injected Guanethidine*[*] *on Cardiovascular Reactivity to Pressor Substances in Dogs*

Drug or Procedure	Control Response, Mm.Hg	Response After Guanethidine, Mm.Hg
Dog 1 (unanesthetized)		
Arterenol	24	72
24 hr. later	120	88
Tyramine	16	28
24 hr. later	30	6
Angiotensin	18	46
Metaraminol	12	34
Dog 2 (pentobarbital anesthesia)		
Arternol	50	88
Tyramine	36	24
Phenylephrine	34	46
Metaraminol	18	38
Vasopressin	8	22
Dog 3 (pentobarbital anesthesia)		
Serotonin	24	—30
Vasopressin	28	56
Angiotensin	40	90
Splanchnic stimulation	110	116

[*] 15 mg. per kilogram of body weight.

Effect on Denervated Perfused Hind Legs of Dogs.—Denervated hind legs of dogs were perfused and the effect on arterial pressure of injection of 5 mg. of guanethidine per kilogram was measured. These experiments were done by Dr. J. W. McCubbin and Y. Kaneko. A sustained rise in pressure within the vessels of the perfused leg occurred, the curve very much resembling that of the pressure in the animal's body. The rise in pressure in the leg continued well after the systemic pressure had returned to, or below, control levels.

Effect on Carotid Occlusion Reflex.—In dogs anesthetized with pentobarbital and after section of the vagus nerves, effect of the drug on carotid occlusion reflex was studied. Immediately after intravenous injection of 5 to 15 mg. of guanethidine per kilogram, the occlusion reflex disappeared; three hours later it was about 50% restored. It could again be abolished by another injection of the material.

Effect on Cardiovascular Reactivity to Pressor Substances.—A variety of pressor substances were tested before and after intravenous injection of guanethidine in both anesthetized and unanesthetized dogs. Examples of the results are given in table 3. Effects of arterenol, angiotensin,[4] vasopressin (Pitressin), and metaraminol (Aramine) were clearly augmented by guanethidine in both anesthetized and unanesthetized dogs. Tyramine, amphetamine, mephentermine (Wyamine), and ephedrine pressor responses were usually depressed. Serotonin response was usually reversed from pressor to depressor. The effect of DMPP (1,1-dimethyl-4-phenylpiperazinium iodide) was reduced but not abolished, and the depression did not last longer than one hour. The pressor effect of stimulation of the peripheral end of the cut splanchnic nerve was not depressed.

Su 4029 in doses of 20 mg. per kilogram blocked the pressor actions of amphetamine, ephedrine, and tuaminoheptane (Tuamine), while it augmented or had no marked effect on arterenol, vasopressin, metaraminol, and 3-hydroxyphenyl ethanolamine hydrochloride. The effect of serotonin was often reversed, or, if depressor, it might become more so. In anesthetized cats the same order of effects was noted, except that the effects of arterenol, angiotensin, and vasopressin were more likely to be clearly augmented.

Short-term Effects of Intravenous Administration in Dogs with Chronic Renal and Neurogenic Hypertension.—Dogs with renal hypertension produced by wrapping the kidneys in cellophane[5] and with neurogenic hypertension induced by section of the buffer nerves were studied without anesthesia. These dogs were prepared by Dr. James McCubbin. Two examples of the effects of intravenously given guanethidine are shown in table 4; the effects on a dog with renal hypertension are graphically illustrated in figure 3. The chief differences in response were that in the dogs with neurogenic hypertension the depressor effect was great and prolonged while in those with renal hypertension it was short and followed by a prolonged pressor response. The effect of serotonin was reversed from pressor to depressor in the dogs with renal hypertension and from depressor to pressor in those with neurogenic hypertension.

Long-term Oral Treatment of Dogs with Renal and Neurogenic Hypertension.—Two dogs with renal and two with neurogenic hypertension were given guanethidine by mouth for periods of about 65 days in doses varying from 200 to 600 mg. (average, 19 to 63 mg. per kilogram). Figures 4 and 5 show the average control intra-arterial blood pressure measurements, those during administration of the drug, and those after discontinuing use of it.

TABLE 4.—*Effect of Intravenously Injected Guanethidine*[*] *on Arterial Pressure of Dogs*

Drug	Control, Mm.Hg	After Guanethidine, Mm.Hg	Response to Guanethidine, Mm.Hg
Dog 1 (renal hypertension—av. B. P. 212 mm. Hg)			
Arterenol	54	88; 102	—68 +54
Serotonin	20	—20	
Dog 2 (neurogenic hypertension—av. B. P. 196 mm. Hg)			
Arterenol	74	84; 106	—116
Serotonin	—6	24	

[*] 15 mg. per kilogram of body weight.

Comment

The short-term effects of guanethidine must be distinguished from the long-term ones. When it was injected intravenously into unanesthetized dogs or those anesthetized with pentobarbital, there was an initial transient fall in arterial pressure followed by a prolonged rise. The rise may not have disappeared after several hours.

Heart rate and cardiac output rose sharply and vasoconstriction occurred in the legs independently of the nervous system. Respiratory rate transiently rose. The carotid occlusion reflex immediately disappeared. The response to arterenol, angiotensin, vasopressin, and metaraminol was augmented, while that to tyramine, amphetamine, mephentermine, and ephedrine was either unaltered or depressed. Serotonin response was usually reversed. The response to stimulation of the splanchnic nerve was not depressed.

The rise in pressure is clearly due to a combination of increased cardiac output and peripheral vasoconstriction, the degree of it being augmented by loss of the buffering action of the carotid sinus reflex. The augmented response to certain pressor agents may mean that the muscles of the peripheral blood vessels are more sensitive to stimulation than normal. The decrease in response to tyramine, amphetamine, and ephedrine suggests, according to Burn and Rand,[6] a decreased secretion of arterenol from the arterial wall, which diminishes the action of drugs dependent on this secreted arterenol for their action. In short, the response to these varied pressor agents is like that which follows treatment with reserpine. This view is strengthened by the quieting effect guanethidine exerts after its intravenous administration.

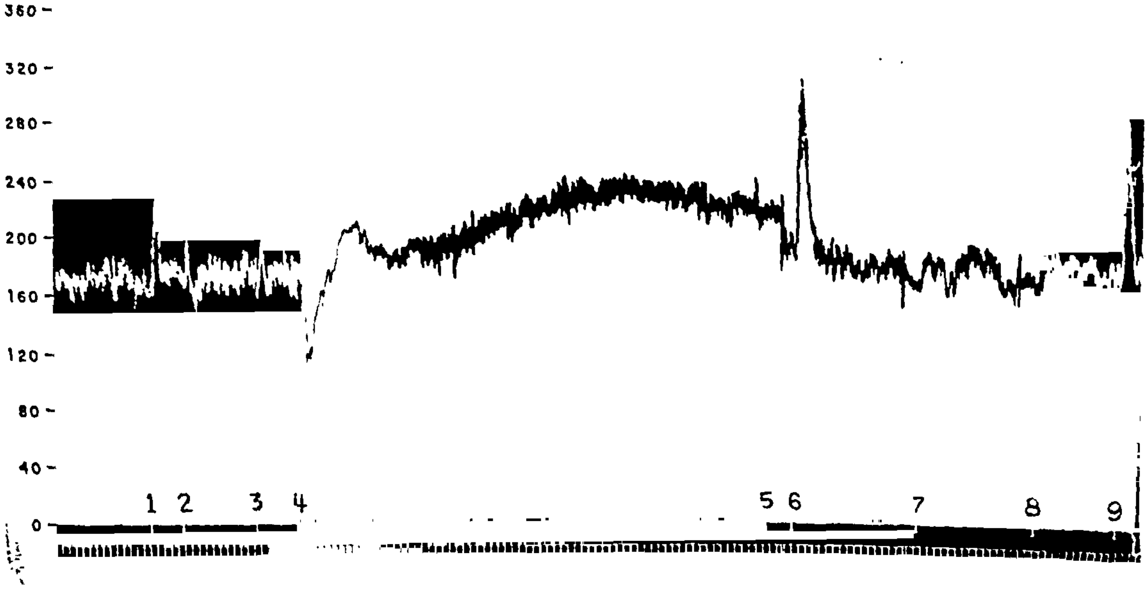

Fig. 3.—Effect of guanethidine on arterial pressure and cardiovascular reactivity in an unanesthetized dog with renal hypertension: (1) arterenol, 10 mcg.; (2) serotonin; (3) ephedrine, 1 mg.; (4) guanethidine, 15 mg. per kilogram of body weight; (5) blood pressure, 222 mm. Hg one hour later; (6) arterenol; (7) serotonin; (8) ephedrine; (9) arterenol. Time, one minute.

Su 4029 had somewhat similar action in short-term experiments. Maxwell and others[7] found that it blocked the hypertensive action of amphetamine and ephedrine. They suggested that it acts on the alpha receptors sensitive to phentolamine and Dibenamine (β-chloroethyldibenzylamine hydrochloride). Our results show blockade of amphetamine, ephedrine, and tuaminoheptane, while effects of arterenol, angiotensin, and vasopressin were augmented, suggesting a common receptor site for the latter group.

The results of long-term treatment of dogs with neurogenic and renal hypertension showed clearly that those with neurogenic hypertension were more responsive to the hypotensive action of guanethidine than the other group, but both responded. After use of the drug had been discontinued, several days elapsed before the arterial pressure started to return toward control levels.

When given by mouth to hypertensive patients, the drug shows none of the actions demonstrated in dogs after intravenous administration. The response of the blood pressure to single test doses of guanethidine given by mouth does not appear to be a reliable guide to the subsequent response after weeks or months.

When the drug was given in a dose range of 25 to 100 mg. daily, arterial pressure slowly fell over a period of several days to a week. Postural hypotension usually appeared before the supine pressure was normal. It has seemed helpful to allow the discomfort of postural hypotension to persist for a number of days in the hope that the patient will gradually adjust to it and will be left with a lower average supine pressure than if the dose were reduced.

Patients with a proved renal arterial lesion have responded seemingly as well as those with essential hypertension. Although tachycardia was a short-term effect in dogs, the patients usually showed bradycardia, which was only slightly influenced by administration of atropine. The drug had little sedative effect.

The only side-effect we have noted so far has been a tendency to slight diarrhea. Two patients have had slight edema, but we do not know whether this was due to the drug.

Summary

The drug [2-(octahydro-1-azocinyl)-ethyl] guanidine sulfate (guanethidine), given intravenously in normal and anesthetized dogs, raises arterial pressure and increases cardiac output and rate. Constriction of the vessels occurs in the denervated perfused leg. The carotid occlusion reflex is abolished. The responses to a variety of pressor substances suggest a reserpine-like action, with diminution of the available arterenol in the blood vessel wall. Long-term treatment of dogs with renal and neurogenic hypertension lowers blood pressure sharply, the more so in the latter group. The hypotensive effect is prolonged.

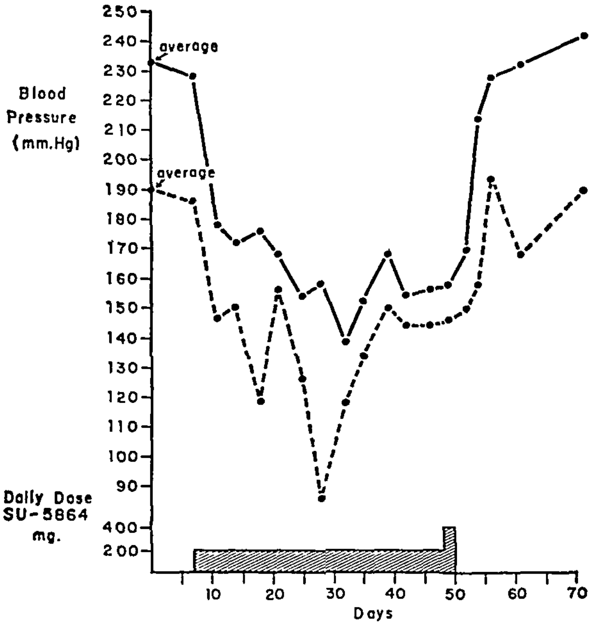

Fig. 4.—Results of long-term treatment with guanethidine of two dogs with neurogenic hypertension. Dot marked "average" represents arterial blood pressures for four weeks before treatment.

Treatment of 18 hypertensive patients with guanethidine shows it to be an effective hypotensive agent, with mild diarrhea as the only side-effect so far noted. The fall in arterial blood pressure is slow and prolonged, often with postural hypotension preceding normal supine pressure. Bradycardia commonly occurs.

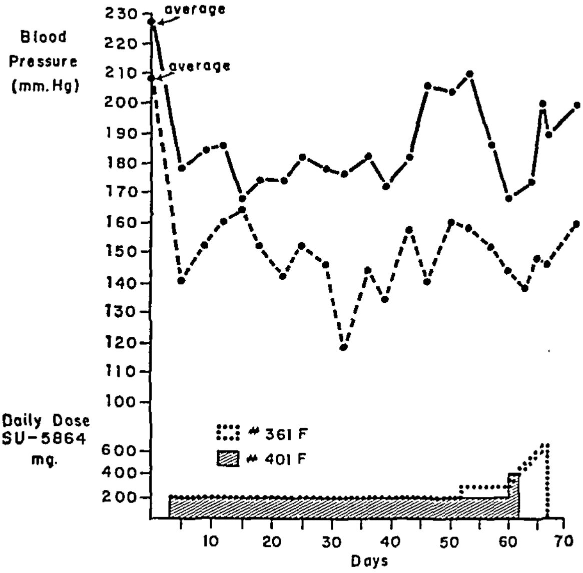

Fig. 5.—Results of long-term treatment with guanethidine of two dogs with renal hypertension. Dot marked "average" represents arterial blood pressures for four weeks before treatment.

Hexahydro-1-azepinepropionamidoxime dihydrochloride was a much less effective antihypertensive agent. The chemical structure and mechanisms of action of guanethidine differ from those of other antihypertensive agents.

Addendum

In future experience guanethidine continues to be a potent, effective antihypertensive drug. Neither tolerance nor toxicity has developed. Diarrhea has been mild and easily controlled. The patient in case 16 is now normotensive after the addition of therapy with hydralazine, 200 mg. per day, and the patient in case 18 has experienced further blood pressure reduction by the addition of therapy with chlorothiazide.

2020 E. 93rd St. (6) (Dr. Page).

The guanethidine used in this study was supplied by Ciba Pharmaceutical Products Inc., Summit, N. J., through Dr. William Wagner.

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CLINICAL STUDIES ON HYDROCHLOROTHIAZIDE—ANTIHYPERTENSIVE AND METABOLIC EFFECTS

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and
Mervyn Sopher, M.D., Cleveland

Hydrochlorothiazide appears to be a potent diuretic as well as antihypertensive agent. Its main action is to produce sodium and chloride diuresis. Ten patients with essential hypertension and one with congestive heart failure were given 50 mg. of hydrochlorothiazide three times a day. The 10 experienced a fall in blood pressure, and the patient with edema had diuresis. The drug was well tolerated by all, and no major toxic effects were noted. Patients were discharged after one week of therapy in the hospital and examined weekly thereafter in the outpatient department. Perhaps the best way to regulate blood pressure in essential hypertension is to admit the patient to the hospital, place him on a no-sodium diet for several days, and then give a general diet along with a sodium diuretic agent.

The value of chlorothiazide as an antihypertensive agent, as well as a diuretic, has been well established.[1] Because of this, interest has been aroused in finding compounds of similar but more potent activity. Hydrochlorothiazide appears to be one of these. It differs from chlorothiazide in that the heterocyclic ring is completely saturated. Animal studies have shown that hydrochlorothiazide is a compound of low toxicity and that it is effective as a diuretic agent in much smaller doses than chlorothiazide. It is our purpose to report the antihypertensive and metabolic effects of this drug in the edema-free hypertensive patient.

Method

Ten patients with stable essential hypertension, who had no clinical evidence of edema and who had been followed for at least one month in the outpatient department, were admitted to the metabolic ward at Mount Sinai Hospital of Cleveland. These patients had had no recent antihypertensive therapy and were on unrestricted diets. In addition, one patient with severe congestive heart failure was admitted to the study. Initial blood pressures, weights, and serum and urine electrolyte levels were determined, and the patients were placed on a 1-Gm. sodium diet.

Serum electrolyte levels and 24-hour urinary excretions of sodium, potassium, and chloride were determined, and observations were continued on blood pressure and weight. When stable base-line values were obtained, the patients were given 50 mg. of hydrochlorothiazide three times a day. After one week of therapy the patients were discharged, to be examined at weekly intervals in the outpatient department. During this time they received the same dose of hydrocholorothiazide and were on general diets. Serum and urine sodium and potassium values were determined by a Beckman flamephotometer. Chloride levels were estimated by the method of Schales and Schales.[2]

Results

The drug was well tolerated by all of the patients, and no major toxic effects were noted. Several patients experienced transient, vague abdom-

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inal discomfort and one developed pruritus. All of these cleared despite continued administration of the drug.

The nonprotein nitrogen level showed a rise in all of the patients, the maximum increase in four patients being over 30 mg.% (32-47 mg.%). In only two patients was the rise associated with an increase in the hematocrit value, and in one both levels fell promptly. In 8 of the 10 patients the nonprotein nitrogen level fell to normal within one week; in 1 it remained stable at a higher level (45-50 mg.%); and in 1 a gradual rise (92 mg.%) was noted during the follow-up period.

Table 1 shows the effect of the drug on blood pressure. All of the patients had a significant lowering, the majority of the average treatment levels being in the normotensive range. The lowest blood pressure is recorded in this table, and it is of significance that hypotensive levels were not reached. During treatment occasional elevated values were noted, independent of the duration of treatment, and some of the elevations occurred late in the course. In only one patient (case 10) did the range of blood pressure reach the pretreatment level during treatment.

Despite the fact that these patients were clinically edema-free, they all experienced an initial diuresis, as shown by weight loss (table 1). This was only a transient phenomenon, and weights returned to pretreatment levels after only a few days in all. The final stabilized weights show some variations from base-line values and are probably not related to the drug.

The patients had numerous serum sodium, potassium, and chloride level determinations during the study. Although the majority of the findings were within normal limits, there was a tendency toward hyponatremia, hypochloremia, and hypokalemia. Table 1 shows the lowest serum value obtained on each patient during the study. The normal serum sodium value is 138-145 mEq. per liter, chloride 98-102 mEq. per liter, and potassium 3.0-4.5 mEq. per liter. Only one patient (case 10) required supplementary electrolytes (because of weakness); levels in all the rest returned to normal without treatment.

Table 2 shows the effects of hydrochlorothiazide on urinary sodium, chloride, and potassium levels. The highest values obtained in the 24-hour urine samples occurred on the first day of treatment. All of the patients had an initial sodium and chloride diuresis, and all but one (case 5) had an initial potassium diuresis. During the follow-up period, six patients maintained the sodium and potassium diuresis and eight the chloride diuresis. Only one patient (case 11) with edema was admitted to the study. He had severe congestive heart failure and lost 40 lb. (18.1 kg.) in weight during his 14-day treatment period with hydrochlorothiazide, 50 mg. three times a day. Although the urinary electrolyte changes in this patient followed the same pattern as in the hypertensive patients, they were of much greater magnitude—especially the urinary sodium excretion.

The figure shows the typical response of a patient (case 6) with essential hypertension and no edema to the drug. The blood pressure response occurs within the first 24 to 48 hours of treatment. This is coincidental with the large diuresis of sodium, chloride, and water, potassium diuresis being only slight. During the next few days, a marked reduction in sodium, chloride, and water excretion occurs.

TABLE 1.—*Laboratory Data on Ten Patients with Stable Essential Hypertension Given Hydrochlorothiazide, 50 Mg. Three Times a Day*

		Blood Pressure, Mm. Hg				Weight, Lb.			Serum Sodium, Chloride, and Potassium Levels During Therapy, mEq./Liter		
			During Therapy				During Therapy				
Case No.	Age, Yr.	Base Line	Lowest	Range	Av.	Initial	Lowest	Stabilized	Sodium	Chloride	Potassium
1	37	180/120	120/80	120-135/80-90	130/85	159	146	151	139	97	3.0
2	45	220/140	110/80	110-160/90-110	135/100	137	132	137	135	90	3.7
3	56	250/110	140/70	140-210/70-100	172/88	136	132	136	134	101	3.8
4	49	180/110	120/70	120-170/70-100	136/87	187	177	185	134	98	3.0
5	47	180/110	110/70	110-140/70-90	121/75	221½	207½	223	139	100	3.6
6	39	180/120	120/75	120-150/75-100	135/84	150	145	150	139	98.5	3.7
7	38	200/100	120/80	120-170/80-100	144/93	111¾	110	115¼	138	101	3.6
8*	27	170/130	130/90	110-140/90-110	144/99	184½	171	171	135	92	3.5
9	43	220/120	110/70	110-180/70-120	150/85	155½	145	145	133	91	3.4
10	48	240/150	160/90	160-250/90-170	205/116	128	122	140	137	92	2.8

* Male patient.

Weight changes and elevation in nonprotein nitrogen level seen on first or second day of treatment return to base-line values. On discharge to the outpatient department and return to a general diet, a sustained sodium and chloride diuresis is present, with only minor changes in potassium and water excretion, blood pressure reduction persisting.

Comment

Hydrochlorothiazide appears to be a potent diuretic as well as antihypertensive agent. Its main action is to produce sodium and chloride diuresis, with minor effects on potassium. All the hypertensive patients in the study had a fall in blood pressure, as well as a sodium and chloride diuresis. The fall in urinary sodium and chloride levels while the patients were on low-salt diet probably represents renal conservation of sodium and chloride in depleted state. On general diets the sodium and chloride excretions were above base-line levels.

In hypertensive patients, the mode of action of the drug could be, in part, related to the sodium diuretic action, depleting the body of sodium stores and perhaps maintaining the patient on a low-salt diet despite general food intake. It has been shown that severe sodium restriction alone will lower blood pressure. Because of the difficulty of placing a patient on severe sodium restriction outside of the hospital, we do not see a fall in blood pressure on the usual low-sodium diets. Perhaps the best way to regulate blood pressure in essential hypertension is to admit the patient to the hospital, place him on a no-sodium diet for several days until his sodium stores are depleted, and then give him a general diet along with a sodium diuretic agent to maintain his low-sodium state.

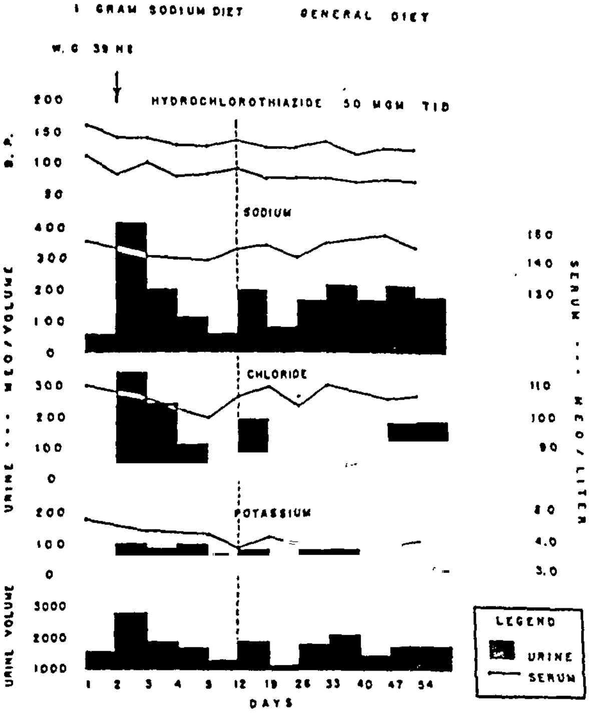
TABLE 2.—*Urinary Changes in Sodium, Chloride, and Potassium Levels Before and After Hydrochlorothiazide Therapy, 50 Mg. Three Times a Day, in Eleven Patients with Stable Essential Hypertension*

	Sodium, mEq./24 Hr.			Chloride, mEq./24 Hr.			Potassium, mEq./24 Hr.		
	Before Therapy,	After Therapy		Before Therapy,	After Therapy		Before Therapy,	After Therapy	
Case No.	Av.	Av.	Highest	Av.	Av.	Highest	Av.	Av.	Highest
1	80	94	209	104	116	254	63	62	83
2	133	130	304	76	116	256	60	79	149
3	94	111	175	106	127	210	27	64	91
4	145	137	338	65	132	277	60	54	73
5	203	92	267	192	99	253	57	39	56
6	56	189	409	31	177	334	56	69	92
7	10	127	190	24	153	217	29	73	88
8	173	108	352	203	98	235	59	75	118
9	34	68	218	22	64	168	62	64	104
10	31	85	198	41	95	190	41	76	113
11*	30	345	626	56	151	253	48	68	97

* 58-year-old man with congestive heart failure.

Summary

Ten patients with essential hypertension and one with congestive heart failure were treated with hydrocholorothiazide, 50 mg. three times a day. All of the patients with hypertension experienced a fall in blood pressure, and the patient with edema had diuresis.



Effect of hydrochlorothiazide on blood pressure, sodium, chloride, and potassium levels, and urine volume in 39-year-old woman (case 6) with essential hypertension and nc edema reaction to drug.

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The hydrochlorothiazide used in this study was supplied as Esidrix by Dr. Robert Wagner of Ciba Pharmaceutical Products Company.

Ruth Katz, Eleanor Susman, and Eva Ray provided technical assistance in this study.

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STAPHYLOCOCCIC WOUND INFECTIONS

STUDY OF WOUND INFECTIONS IN SEVERAL THOUSAND HERNIA CASES

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Extensive study of possible causes of wound sepsis revealed that the two most common were virulent staphylococci in nasal carriers among operating room team personnel and airborne pathogens in the operating room. If a surgeon finds he has an epidemic of infections, he should first of all consider himself as a possible source. A special mask patterned after the oxygen mask used by airmen is useful if the surgeon is found to be a source of infection. Ultraviolet light was found of value for air sterilization but not for skin sterilization. Studies showed that benzalkonium swabbing of the skin leaves much to be desired, but the patient's skin, in 182 cases observed, appeared to play only an insignificant role in wound sepsis under the given conditions. More efficient masking of the operating room personnel and general measures to insure maximum cleanliness are suggested as means for decreasing the frequency of surgical infections.

An analysis of current literature reveals that wound sepsis is prevalent and at times reaches epidemic proportions.[1] The number of articles that have appeared in the literature on this subject over the past few years and the necessity of actually closing some operating theaters for indefinite periods in various parts of the world are indicative of its universal importance.

Subjectively, discomfort assumes first priority in the acute stage of wound sepsis, while protracted convalescence with discharging sinuses in the chronic stage may, in certain instances, burden the patient with considerable economic difficulties. "The cost in both health and money of infection contracted in hospital is difficult to assess but is certainly very great."[2]

This subject has already been covered from many aspects in recent literature, and yet there is still an air of uncertainty and some difference of opinion about the relative importance of many factors concerned. The purpose of this article is not to attempt an inquiry into all compartments of this broad field but rather to relate our experience of wound sepsis at Shouldice Surgery and the information gleaned from the investigations carried out with emphasis chiefly on pathogenesis. With the existing information already voluminous, it is difficult to write on a subject of this kind without being somewhat repetitious, but several aspects of the problem will be considered and, where possible, definite conclusions drawn.

A rather sharp increase in the wound infection rate early in 1954 was the stimulus for intensification of this study, as this occurred in only one of our two private hospitals. An additional feature noted was a relative increase in the number of severe infections. While most were classified as being of moderate severity, there were a few cases characterized by a wide margin of surrounding cellulitis, extending for some distance beyond the actual site of drainage, and an accompanying marked constitutional reaction, a matter of some concern to those in charge. It was obvious that the pathogen involved was a particularly virulent one, and the occurrence of cutaneous infections in a few members of our hospital personnel about the same time served as further evidence of this. On the other hand, a few of the infections were clinically mild and barely worthy of the name, except from a bacteriological point of view, and for the purposes of this study they were included. With some fluctuation the infection rate remained elevated for about 18 months, until the pathogenesis was clarified and definitive prophylactic measures instituted. It is this period which has been most extensively investigated, with indispensable assistance from the Ontario Provincial Central Laboratory.

Shouldice Surgery consists of two hospitals, A and B, separated by a distance of about 10 miles, but only in the latter was the increased infection rate noted, thus affording a unique opportunity for study. Why a higher infection rate prevailed in the one hospital was a mystery for some months. There were few variables, however, and this allowed hospital A to serve as a control—an ideal one in that preoperative and postoperative care of patients, sterilization of instruments, and surgical technique were almost identical in both places. Furthermore, all patients underwent operation only for the radical cure of hernia, and the vast majority of the hernias were in the inguinal region. Even most of the personnel did not constitute variables in the problem, as there was frequent exchange of help between the two hospitals. Finally, nearly all cases could be con-

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From Shouldice Surgery.

sidered surgically clean. This limited, appreciably, environmental contamination with heterogeneous groups of organisms and simplified the bacteriological investigation.

In the beginning it was thought that the first few infected persons, by contaminating the surroundings, might have provided a reservoir for subsequently infecting clean surgical wounds. It could be shown by exposing blood agar plates that the room in which a patient with a discharging wound resided rapidly became laden with pathogenic staphylococci and similar pathogens could be recovered from various sources throughout the hospital, such as dust and debris obtained from vacuumed rugs. Extensive efforts were made to solve this alarming problem, and the various investigations that were conducted will now be considered.

Techniques for Antisepsis

Antiseptics.—An alcohol solution of benzalkonium (Zephiran) chloride for preoperative preparation of the skin had been used routinely for some time, and an attempt was made to measure its effect on the patient's flora. Prior to its application in 23 patients, swabs of the inguinal region were taken and planted immediately on blood agar plates. In 22 (96%) of these cases micro-organisms were grown and in 2 (9%) pathogenic staphylococci were found. After the application of two coats of the alcohol solution of benzalkonium chloride in a group of 83 patients, swabs were taken, and in 50 (60%) growth was obtained, with 6% yielding pathogenic staphylococci. From this same group of patients skin swabs were again taken postoperatively, and in 73 (88%) growth was obtained, with 7% yielding pathogenic staphylococci. Thus, the incidence of residual micro-organisms during the course of an average operation rose from 60 to 88%. This suggests that the initial activity of benzalkonium chloride, leaving much to be desired, is most marked shortly after application and rather rapidly loses its effectiveness thereafter. These observations undoubtedly hold true to some extent for other antiseptic agents in current use. It must be pointed out, however, that on no occasion have we been able to recover from the infected wound staphylococci identical to those present on the patient's skin preoperatively. The latter must rarely cause wound sepsis and, furthermore, it is likely that most people develop an immunity to their own skin flora. Nevertheless, during each operation at this institution skin towels are applied to the wound edges, with use of many small towel clips, and this procedure would seem likely to further minimize the danger of any infection of the wound by skin bacteria.

In 116 patients the subcutaneous tissues of the wound were swabbed after suture of the external oblique aponeurosis. In swabs from two of these, pathogenic staphylococci were grown, and one patient later developed clinical infection. The other patient was receiving, prophylactically, chloramphenicol (Chloromycetin). No infection occurred in the remaining 114 wounds, in which no pathogens could be demonstrated at the time of closure. Hence, clinical infection would seem more likely to occur if pathogenic organisms can be demonstrated in the wound. It seems only reasonable, however, that some degree of bacterial contamination takes place during every operation of appreciable duration. In a total of 182 patients postoperative skin swabs were taken. In 10 of these swabs, pathogenic staphylococci were grown. Of the latter patients, only one developed clinical infection, and in 9 of 17 patients with clinical infection skin swabs had been taken at the time of closure but in only one were pathogenic staphylococci demonstrated. These findings again suggest that the host's skin probably plays an insignificant role in the pathogenesis of wound sepsis.

Punctured Gloves.—It has always been the practice in this institution to make a note of any gloves punctured during an operation. With the use of wire, as compared to more flexible suture materials, a higher puncture rate is to be expected. Over a period of several days, 150 gloves were carefully checked immediately after the completion of operation. When they were inflated with air and placed under water, air bubbles revealed some leakage in 61%. In an effort to determine what role such punctures might play in the pathogenesis of wound sepsis, swabs from the inner surfaces of eight pairs of gloves from the surgical staff were streaked on blood agar plates at the completion of operation. While admittedly few were tested, pathogenic growth was never obtained.

More recently, the following work has been carried out[3]: On 75 occasions, immediately after the completion of operation the insides of the gloves and the hands were swabbed and the swabs were plated at once on blood agar. This series included gloves worn by all members of the surgical team. From 126 gloves (83.4%) no growth was obtained. From the remaining 24 gloves only nonpathogenic growth was obtained. From no glove was a colony of coagulase-positive hemolytic staphylococcus grown. Similar swabs were taken from the outside of a large number of gloves toward the end of a series of operations. Gloves from all members of the operating team were tested. In 91.4% no growth was obtained, and in the remaining 8.6% only nonpathogenic growths could be demonstrated. The failure of these investigations to demonstrate the presence of coagulase-positive hemolytic staphylococci, the organisms responsible for almost 100% of our series of infections, would indicate that, under ordinary operating room conditions, the surgical team's hands are a negligible source of wound sepsis.

The Surgical Scrub.—As noted above, the surgeon's hands were investigated immediately after removal of gloves on completion of operation and no hemolytic staphylococci were demonstrated. At the same time it could be shown that after the surgeon handled a dressing from an infected wound pathogenic growth was easily obtained from the hands. However, after he washed his hands with ordinary soap and water no pathogenic organisms could be cultured. It seems, therefore, that the skin of the hands can be easily cleansed of any contaminating pathogens, and the specific technique used for cleansing purposes would seem to be of relatively little importance. While the mechanical effect of the brush is probably more important than the bactericidal effect of the soap, vigorous and prolonged scrubbing, which often results in injury to the skin, would not seem to be justified. Scrubbing of the hands and arms has for some time been limited to two minutes at Shouldice Surgery.

Surgical Instruments.—By similar investigation, wound sepsis could never be traced to contamination of surgical instruments. In each case indicators showed that sterility had been achieved. Furthermore, several spot checks of instruments were carried out but pathogenic growth was never obtained. This also would seem to be a negligible source of wound contamination.

Table 1.—*Results on Culture of Nasal Swabs from Hospital Personnel*

Subject No.	Swabs	
	No. Taken	No. Positive*
1	18	13
2	12	0
3	11	1
4	14	13
5	9	3
6	13	13
7	7	0
8	13	12
9	12	0
10	13	11
11	8	1
12	8	1
13†	16	8
14†	12	7
15†	8	0

* Coagulase-positive hemolytic staphlyococci (potentially virulent staphylococci).
† Surgeons.

Surgical Technique.—As for surgical technique itself, hematoma formation and rough dissection must be considered as predisposing factors in that blood and devitalized tissues are excellent culture mediums. In this regard, however, it was often the patient with an easy, straightforward case rather than one with a long tedious recurrence who became infected. This would support the view that the implantation of virulent bacteria in the wound during the course of an operation is the principal factor leading to clinical infection.

Nares and Airborne Bacteria

That nasal carriage might be responsible for the epidemic was also considered, and all operating room personnel were investigated on several occasions. Swabs of the nares were taken and plated immediately on blood agar. In this connection it was found that only rarely were staphylococci recovered from the mouth or pharyngeal wall proper. This is in keeping with the findings of Hare and Thomas.[4]

In table 1 are listed the results of nasal swabbing in 15 members of the staff. The number of swabs obtained from each person varied from 7 to 18. It will be noted that in four of the members, including one surgeon, coagulase-positive hemolytic staphylococci were not recovered on any occasion; two of these persons worked exclusively at hospital B, where the epidemic was taking place. In three members, only one positive swab for each was obtained. On the other hand, in four members almost consistently positive results were obtained for nasal pathogenic staphylococci. The remaining four were in an intermediate position in that, on the average, about one-half of their swabs were positive.

These four groups would seem to fall roughly into the patterns of nasal carriage described by Duncan and co-workers,[5] i. e., constant, intermittent, occasional, or noncarriage. The immunological significance of this variation in nasal carriage is not known. In any event, it is difficult to understand how some persons can resist colonization indefinitely, even in the presence of a heavily contaminated environment, while others cannot. From a bacteriological point of view, the idea of the noncarrier would seem to be a myth, in that it is highly unlikely that such a person does not at some time or another harbor nasal pathogens. It is undoubtedly just a matter of timing before swabbing and carriage coincide, and, therefore, occasional carriers and noncarriers should be included in the same category. It follows that the nose in these persons must, of necessity, play an insignificant role in the pathogenesis of wound sepsis. On the other hand, constant and intermittent carriers are always a threat and play a major role in wound contamination and sepsis.

Early attempts to correlate nasal carriage and wound sepsis, despite bacteriophage typing of the organisms, were unsuccessful. In the first place, several members of the staff were shown to be nasal carriers, but, more important, it was not until well on in the study that the organism responsible for most of the infections could be identified by bacteriophage typing. Hence, at first, it was impossible to incriminate any one person, and the enigma was all the more perplexing in that there were just as many nasal carriers at hospital A, where the incidence of sepsis was still low.

Airborne Pathogens.—The role that airborne pathogens might play in the pathogenesis of wound sepsis was also investigated, and blood agar plates were exposed during many operations. During 91 (26%) of 346 operations, coagulase-positive staphylococci could be demonstrated. Of the 91 wounds 9 (10%) became infected, whereas of the remaining

255 wounds only 10 (4%) became infected. Thus, on a percentage basis, there were over twice as many infections in those patients whose operations were performed in the presence of demonstrable pathogens.

Blood agar plates were exposed in the operating room at some time during each morning for 143 days. On 61 days coagulase-positive staphylococci could be demonstrated in the air, and during this period 13 of the patients developed wound sepsis (21%). On the remaining 82 days pathogenic staphylococci could not be demonstrated in the operating room air, and during this period only six patients developed wound sepsis (7%). Since the same number of operations was performed daily, these figures indicate that wound sepsis occurred three times more frequently in the presence of demonstrable pathogens in the air of the operating room.

In 11 of 17 clinical infections (65%) pathogenic staphylococci had been demonstrated in the operating room sometime during the morning of each operation. Thus, in 65% of cases, the evidence was at least suggestive that infection could have occurred in the operating room. That this was the case in most, if not all, cases of infection during the period of elevated infection rate was later proved beyond any reasonable doubt.

In most patients the wound edges are sealed by fibrin a few minutes after departure from the operating room. This plus the additional protection of a sterile dressing would seem to afford an effective barrier against subsequent bacterial invasion. While it is true that minimal oozing continues for longer periods in some patients, it seems unreasonable that such minimal exposure is responsible for more than an occasional septic wound.

That a patient might be responsible for infecting his own wound was also given consideration, especially after it was demonstrated that about 30%, on admission to hospital, were carrying coagulase-positive staphylococci in their noses. Hence, for a period of time they were actually masked during their stay in the operating theater, but no significant change in the infection rate occurred. Furthermore, in 16 of 17 patients with clinical infections nasal swabs had been taken prior to operation. Pathogenic staphylococci were recovered from the nose in four of the patients, but in three the organisms were found to be sensitive to penicillin, whereas those from the wounds were resistant. It would seem, therefore, that even a patient who is a nasal carrier is rarely responsible for sufficient contamination of the operating room air to infect his own wound.

Source of Infection and Solution of Problem

Quite fortuitously, it was not until surgeon 1 (table 1, case 13) at hospital B and surgeon 2 at hospital A exchanged positions that the riddle was solved, at least from a pathogenic point of view. The infection rate at hospital B fell immediately, whereas surgeon 1, now operating in hospital A, was associated with nine wound infections in operations on 10 consecutive days. From the epidemiology it is certain that he alone was responsible. He shared one of the two operating rooms at hospital A with surgeon 4 (table 1, case 15), who performed an approximately equal number of operations during the same period without a single infection and had always had an excellent record in regard to low incidence of wound sepsis. In the schedule for this 10-day period, four patients were assigned to their room daily. Surgeon 4 performed the first two operations and surgeon 1 the last two. There was a free interchange of assistants and scrub nurses, so that for all practical purposes the surgeon was the only variable. That surgeon 1 had, in effect, a daily infection and surgeon 4 a perfect record, coupled with the decreased rate of wound sepsis in hospital B while surgeon 2 was there, seemed clinical proof enough that the surgeon in question was infecting the operative wounds of his patients.

The fact that this mechanism took place was confirmed bacteriologically. About this time the department of health reported the finding of a new virulent Staphylococcus, which by means of bacteriophage technique was labeled type 81. It is unfortunate that this discovery of type 81 was made late in our clinical investigation, for the same organism was demonstrated in the current infected wound cultures while those from earlier cases were not available for retyping. Earlier bacteriophage typing had not been helpful in isolating the carriers. However, in retrospect it seems likely that type 81 was also the chief invader of the earlier wounds. In support of this contention is the fact that material from 10 current consecutive wound infections was subjected to bacteriophage typing. Eight of the patients had been operated on by surgeon 1, and, of these, in seven type 81 was present in the wound. Surgeons 2 and 4 each had one sporadic infection, but neither wound yielded type 81. These findings again directed attention to the nose, and the entire staff was investigated for this pathogen. Most of the subjects were checked several times, but surgeon 1 was the only person shown to carry it regularly. It was recovered from his nose on 22 out of 37 occasions, and it was evident, both clinically and bacteriologically, that he was responsible for the elevated infection rate. Almost certainly the mechanism involved was direct transmission of pathogens from nose to wound. It was thought by some that this surgeon's tonsils might have been the source of staphylococcic contamination, and tonsillectomy was performed. However, there was no apparent improvement in his infection rate until other prophylactic measures were instituted. Hence, surgeon 1 was relieved of his duties in the operating room until effective prophylaxis could be instituted.

In table 2 is tabulated the number of operations and infections for the four surgeons studied during this period. For surgeons 2 and 3 the infections have been further subdivided according to the hospital in which they occurred. Other operations performed by occasional surgeons were not included in this series, as they were relatively few in number and did not enter into the problem. It should be noted that (1) while the over-all infection rate for this period was 2.2% it varied from 1.0% to 7.3% for individual surgeons, (2) surgeon 1 had an infection rate of 7.3% whereas the others had an incidence of less than 2%, and (3) surgeons 2 and 3 both had a relatively high rate at hospital B but lower than average at hospital A. Indeed, surgeon 2 performed some 600 operations at hospital A with only a single recorded wound infection; of his eight patients who developed sepsis at hospital B, surgeon 1 had assisted in five.

After the removal of surgeon 1 from the operating room, surgeon 2 performed 117 consecutive operations at hospital B without a wound infection. Even more striking is the fact that surgeon 3 was assisted by surgeon 1 on all 11 patients at hospital B who subsequently developed infection. Furthermore, except in rare instances surgeons 2 and 3 were not assisted by surgeon 1 when operating at hospital A. These variations in the incidence of wound sepsis for individual surgeons and hospitals have been subjected to statistical analysis and found to be significant. It must be concluded, therefore, that a virulent nasal carrier may be a serious threat to the clean surgical wound. While the danger is greatest when the person functions as surgeon, this study indicates that it is only slightly less when he acts as first assistant.

TABLE 2.—*Correlation of Infections with Hospitals and Surgeons*

	Operations, No.		Total Infections		Infections			
					Hospital A		Hospital B	
Surgeon No.	Hospital A	Hospital B	No.	%	No.	%	No.	%
1	74	444	38	7.3				
2	620	181	9	1.1	1	0.2	8	4.4
3	779	209	19	1.9	8	1.0	11	5.0
4	1,407	0	14	1.0				
Total	2,880	834	80	2.2				

In the case of surgeon 1, the nasal carrier, ordinary masking was obviously not adequate. Hence, efforts were directed along channels that would provide more protection for the open wound or, in other words, prevent direct spread of pathogens from nose to wound. After some trial and error with various types of masks, one providing the necessary protection was designed by one of us (E. E. S.) in 1955, and surgeon 1 has been wearing this ever since. The influence on his infection rate has been remarkable. For over two years he has been doing nearly all the operations at hospital B, and, except for a short period early in 1957 when it was found that the mask had loosened, the infection rate at this hospital has not been significantly different from that at hospital A. During 1956 and 1957 surgeon 1 performed 2,023 herniorrhaphies; infection occurred 29 times, giving him an infection rate of 1.4%. The over-all infection rate for both hospitals in 1956 was 1.12% in 3,124 herniorrhaphies and in 1957 1.2% in 3,303 herniorrhaphies. It is thus evident that the special mask has reduced surgeon 1's infection rate to a level comparable to the rates of other surgeons on the staff.

The mask is similar in appearance to that worn by airmen.[6] In essence, it consists of a facepiece that covers the nose and mouth and fits snugly to the skin, so that there is no escape of air around the margins. It is equipped with a valve in the mouthpiece so that air can be inspired but not expired through the mask itself. Extending from the mask is a length of rubber tubing which rests over one shoulder. Expired air is eliminated through the end of the tube behind the surgeon and away from the wound itself. Originally a bacterial filter was incorporated in the tubing, but the resistance it offered to expiration necessitated removal. Bacteriological investigation at the time failed to show the presence of any pathogens on the filter, so that, apparently, any bacteria present in the expired air settle out along the length of the tubing and fail to contaminate the operating room air. In any event, removal of the filter has been followed by no apparent untoward effects.

More recently, under quiescent conditions, investigations were carried out on airborne pathogens and nasal carriage to see which factor was the more important. To assess the presence and amount of airborne pathogens, blood agar plates were exposed in the operating rooms for one hour each day. The experiment was repeated on several consecutive days. Twenty-five per cent of the plates were positive for pathogenic staphylococci. While this was a rather crude method, it at least demonstrated that pathogenic staphylococci are frequently present.

As for the surgeons' noses, an attempt was made to reproduce operating room conditions as closely as possible with the exception that no mask was worn. Rather than swabbing the nose, the surgeon was required to breathe through his nose onto a blood agar plate held about 6 in. away. This was carried out in a quiet room to eliminate contamination with airborne pathogens as much as possible. It was soon found that, under such conditions, no pathogenic growth was being obtained; therefore the surgeon was then required to expire forcibly through his nose once every minute. Approximately one-half of the plates were exposed for 10 minutes and the remainder for a total of 20 minutes (5-minute periods between operations). In table 3 are recorded the results of this study. That surgeon 1 had the greatest incidence of positive plates was not surprising, in view of the role he played as a nasal carrier in the epidemic at hospital B. However, surgeon 3 was a close second, even though his infection rate had always been low except for the period at hospital B during which he was assisted by surgeon 1. It seems reasonable, therefore, that a nasal carrier of coagulase-positive hemolytic staphylococci is not necessarily a serious threat to the wound. What is likely more significant is the virulence of the specific subgroup of Staphylococcus carried. To date, the only accurate way of assessing this virulence is by means of clinical investigation. Bacteriophage typing, particularly with greater experience, may give further guidance in this regard. In general, the low incidence of positive plates was rather surprising since the experiment was carried out without masks. These findings are similar to those of Hare and Thomas [4] and might well indicate that too much credit has been given the ordinary cloth mask in protecting the wound from the nose. It seems likely that a noncarrier surgeon could operate without a mask and yet not alter his infection rate. We must assume, however, that ordinary masking affords some protection; how much is difficult to say. Certainly, the practice of wearing a mask over the mouth, leaving the nares exposed, is next to useless and should be condemned.

TABLE 3.—*Results of Breathing Through Nose on Blood Agar Plates for Ten to Twenty Minutes*

Surgeon No.	Total No. of Plates	Plates with Coagulase-Positive Hemolytic Staphylococci	
		No.	%
1	58	8	14
3	29	3	10
4	59	2	3
5	48	3	6
6	48	0	0

There can be no doubt that bacteria can and do fall into the open wound during the course of most, if not all, operative procedures. In support of this contention blood agar plates were exposed in the operating room after all operations had been completed. Each day two plates were exposed on the operating table. One was placed at the head of the table and the other under the large overhead lamp, which was left burning. Both plates were left exposed for one hour, and a total of 50 plates was exposed at each site. Conditions did not vary from those existing during an operation, except that there were no people in the room and no operation going on and, thus, activity within the room was less and air contamination by personnel minimal. While only one plate grew coagulase-positive staphylococci (1%), as compared to an incidence of 25% during operating conditions, all plates showed a mild to heavy growth of nonpathogens, indicating that airborne micro-organisms may readily settle in an open wound. The plates under the main operating room light were all contaminated, showing that any up-draught of air created by the heat from this lamp is not sufficient to prevent bacteria from falling into an operative wound.

Ultraviolet Light and Air Sterilization

In the past, ultraviolet light has been criticized as being a relatively poor sterilizing agent because of its inability to penetrate dust particles. Nevertheless, our studies have indicated that it is a good method for clearing a room of its airborne bacteria. Consistently heavy growth was obtained on blood agar plates exposed for an hour in a room which a person with an infected discharging wound had just left, while consistently little or no growth was obtained after a short exposure (one to five minutes) of the same air to ultraviolet radiation. Because of the deleterious effects of such rays on the eyes and skin of operating room personnel, it is not practicable to continually irradiate the entire operating room during an operation. However, it would be easy to arrange lights so that, when on, they would fully irradiate the air of the operating room. These lights could then be switched on for one to five minutes between operations when the room would be unoccupied. Thus, the air would be bacteriologically cleansed between operations and the bacterial content of the air would not increase during the operating room day, as it tends to do if no such special precautions are taken.

In a considerable number of tests at hospital B it was found that blood agar culture plates exposed in the operating room for equal periods of time would show little or no growth the first thing in the morning after ultraviolet lights at floor level had been fully irradiating the room all night but after operations had begun and as the morning progressed the growth on the culture plates became increasingly greater. Adams [7] found a similar situation in his studies. This strongly suggests that the operating room personnel themselves are contaminating the operating room air. This is a situation which is difficult if not impossible to control by ultraviolet irradiation or ventilation measures alone. However, the use of ultraviolet irradiation of the whole operating room air between operations would cut down the count and allow each operation to start fresh with bacteria-free air rather than with air accumulating contamination from all the previous procedures in that room.

Ultraviolet light was also tested as a means of sterilizing the skin. It was not as effective as two coats of the alcohol solution of benzalkonium chloride, even though the skin was exposed to the point of erythema. It is, therefore, of no value for this purpose.

Sporadic Versus Epidemic Sepsis

By definition, sporadic sepsis occurs infrequently in any large series of consecutive operations. Owing to this infrequency and the fact that any one of a number of factors may be involved in the pathogenesis, investigations of such infections are difficult. In general, one might say the greater the incidence of sepsis the more obvious its pathogenesis. Excluding the epidemic period, our infection rate has shown a remarkable constancy from year to year. Furthermore, excluding surgeon 1, the records for individual surgeons have only varied from approximately 0.5 to 1.5%. Thus, an infection rate of plus or minus 1% represents sporadic sepsis for this institution. In other words, one can say that, under the present circumstances, an infection rate of approximately 1% appears to be inevitable in any future period. Constancy is a characteristic feature of sporadic sepsis.

One might criticize any further discussion of this matter by pointing out that the figures quoted represent an excellent record. However, it is felt that an even better record could be achieved by institution of additional prophylactic measures. In addition, it must be remembered that these figures are not strictly comparable to those of a general surgical unit. While at this institution the annual number of open operative wounds is relatively great (3,317 hernia operations in 1957), the hospital is relatively small (50 beds) and the hospital personnel is also relatively small. This limits to some extent the problems of nasal carriage and airborne pathogens. Also, we deal with only clean hernia cases and have no place for patients with varied nonsurgical infections who from time to time require admission to a general hospital. These differences can adequately explain the generally higher infection rates quoted in the literature, so that a figure of 5% or more, which would seem to prevail in many general surgical institutions, is not surprising.[1] Determination of whether a given incidence represents sporadic or epidemic sepsis is somewhat arbitrary and depends to a great extent on what is usual for the institution involved. From a practical point of view, the actual numbers involved are more important than this distinction. Regardless of the institution, an infection rate of 5% or more is appreciable and demands investigation with the object of introducing better prophylaxis.

A sound appreciation of the factors responsible for wound sepsis is required before adequate control can be instituted. Before considering these, it must be pointed out that, while it is convenient to consider the problem in terms of sporadic and epidemic occurrence, the mechanisms involved are frequently identical. Indeed, transition from sporadic to epidemic incidence often represents but accentuation of one or more preexisting factors. The two cannot be divorced, so that discussion of one must, of necessity, include the other.

Comment

It has been assumed that the vast majority of wound infections are seeded in the operating room, and several factors which might conceivably play a role in their pathogenesis have been considered. While breaks in technique, rough handling, the nature of the patient's skin, and similar factors might all be responsible for an occasional infection, the impression gained was that in the over-all picture they play an insignificant role and there is little doubt that some of them have been grossly exaggerated as sources of wound sepsis. It is our opinion that nasal carriage and airborne pathogens are by far the most important factors, but the relative importance of each is not easy to assess. Nasal carriage in the person of surgeon 1 was undoubtedly the chief, if not the only, factor responsible for our epidemic. However, this was the first time in the history of the institution that a nasal carrier had been responsible for wound sepsis of this incidence, so that such a person would seem to be the exception. On the other hand, there are well-documented studies of epidemics due to airborne pathogens, and, even in our investigation, it will be recalled, the infection rate was higher when staphylococci could be demonstrated in the operating room. One must postulate, therefore, a proportional relationship between airborne pathogens, nasal carriage, and wound sepsis. There is no doubt that one can acquire nasal pathogens from a contaminated environment, and it seems certain that recontamination of the air from a carrier's nose can likewise occur. This ping pong exchange of organisms between the air and the nose undoubtedly maintains contamination in a hospital for long periods of time. The nasal carrier is an important source of pathogens who constantly replenishes the hospital reservoir, and this chain reaction may go on indefinitely.

At the time of most intensive study, it was noted that there were several periods during which operating room air contamination and wound sepsis simultaneously increased and there was some evidence, at various times, that this may have been related to the readmission of patients with discharging wounds. Mention has already been made of the rapid environmental contamination in the neighborhood of such a wound. This persists for the patient's entire stay and for some days after his release from hospital, adding to the number of airborne pathogens, influencing nasal carriage, and contaminating, on occasion, clean surgical wounds—thus setting in motion a vicious cycle. This variation in the concentration of airborne pathogens from week to week, day to day, or even during the course of a surgical operation may well govern the hit and miss occurrence of sporadic wound sepsis in individual cases.

That the hospital atmosphere is not the only source of nasal contamination is suggested by a study carried out by and on one of us (C. J. M.). Repeated nasal swabbing had revealed this person to be an apparently constant carrier of coagulase-positive staphylococci. In due time, however, it was discovered that while she was away from home for a few days her nasal swabs would be negative for pathogenic staphylococci but on her return they would just as quickly become positive again. It was then discovered that another member of the family, with multiple nasal polyps, was a constant nasal carrier of potentially virulent staphylococci of a similar bacteriophage type to her own, as far as could be determined. This experiment suggests that contamination of the nose can occur away from the hospital environment and could also be one explanation as to why some persons are only occasional carriers. This would seem to indicate that no one can be certain that, at times, his nose is not being contaminated by environmental conditions. In view of this it would seem clear that all persons in the operating room should have their noses efficiently masked, even though most of their nose swabs are negative.

In an assay of the results of the various investigations already discussed, it is still not possible to determine definitely which factor predominates in the pathogenesis of sporadic (occasional) wound sepsis. The relative importance of nasal carriage and airborne organisms must vary from time to time and place to place according to existing conditions. As we have shown, a serious outbreak of wound sepsis can result from the presence of a single nasal carrier of virulent staphylococci at the operating table. In support of the airborne mechanism, on the other hand, is the fact that our infection rate is significantly lower than that of most general hospitals, and a comparison of the respective pathogenic reservoirs can readily explain this difference. It is an established fact that a large percentage of the staphylococci isolated from general hospital wounds are penicillin-resistant, and, of these, bacteriophage type 81 is assuming increasing importance. On the other hand, the vast majority of sporadic infections encountered in this institution seldom yield penicillin-resistant staphylococci, and, apart from the epidemic, type 81 has only rarely been isolated.[8] Although this is pure conjecture, it seems reasonable that minimal contamination with such an organism as type 81 is sufficient to cause sepsis in many wounds. Thus, air heavily contaminated with this and organisms of similar virulence would be a much greater threat than that in which other less virulent pathogens predominated. At any rate, the proportion of airborne pathogens to nonpathogens in most general hospitals must, of necessity, be higher, and this could well explain the greater wound sepsis rate in such institutions.

It is rather amazing that wound sepsis is not more prevalent, and this must indicate a high degree of natural resistance in most persons. At the present time, there is no immunological test that can, in any way, measure a patient's resistance to staphylococcic infection, and clinically it is impossible to predict, except in a general way, those patients who are susceptible. There is little doubt, however, that chronic debilitating disease can interfere with humoral and local defense mechanisms, thus facilitating pathogenic growth. In our own experience, although they have been few in number, there have been more bilateral infections than could be explained by chance. Lowered host resistance is suggested by the facts that the vast majority of these patients exhibited some evidence of chronic ill health, the two operations were never done on the same day, thus tending to discount other factors, and operation on the second side was not always performed by the same surgeon. It may well be that in some cases host resistance is more important than the amount or kind of contamination in determining whether sepsis will ensue.

This work clearly demonstrates the difficulties involved in singling out those nasal carriers who are important in the pathogenesis of wound sepsis. While it is true that the majority of people at times carry coagulase-positive hemolytic staphylococci in their nasal passages, for the most part these organisms are of relatively low virulence and must rarely cause clinical infection. In this study, the only way the surgeon carrier was isolated was by moving him about from one hospital to the other, clearly demonstrating that he was uniquely associated with an increased incidence of infection. At first, nasal cultures and bacteriophage typing were not helpful, but since the identification of bacteriophage type 81 we can say with justification that anyone carrying this micro-organism is carrying one of proved clinical virulence. Several other epidemics in various parts of the world have also been proved due to this organism.[9] The only other laboratory procedure that might be helpful in this regard is based on the observation that, when nasal swabs from the proved surgeon carrier were plated on blood agar, the growth of coagulase-positive hemolytic staphylococci was consistently heavy as opposed to occasional isolated colonies, which was the usual finding in other personnel. Certainly, an accurate laboratory test for the detection of clinically dangerous nasal carriers would be a great help in reducing the incidence of surgical infections.

Recommendations for Control of Sepsis

To be effective, any program of control requires the full cooperation of all surgical services and at least one representative from each service should be appointed to investigate the problem. Specific prophylactic measures will now be considered.

Nasal Carriers.—It would seem that some 50% of personnel of any hospital carry nasal pathogens, even under quiescent conditions. Many of these people undoubtedly harbor pathogens identical to those present in many wounds, but to exclude them from the operating theater would be highly impractical.

Likewise, in a large general institution use of a special mask similar to that already described would be cumbersome. With further work, however, a more comfortable mask could probably be designed.

An outbreak of wound sepsis due to virulent nasal carriage must, of necessity, be local in character, and it is under such circumstances that nasal investigations have a definite place. To be of any value, however, the investigation must include bacteriophage typing of pathogens.

The fact that we have proved a surgeon to be a nasal carrier of virulent staphylococci and the cause of a serious outbreak of wound infections is of great interest. It indicates that such a surgeon, unsuspecting and unprotected, is a serious threat to the clean surgical wound. Because of his proximity to the wound, a surgeon-carrier is more dangerous than a carrier anywhere else in the operating room. These considerations lead us to believe that in any epidemic of wound sepsis, and particularly in a local one, the operating surgeon should be carefully investigated to establish whether he may be a carrier of particularly virulent organisms; if he is, such measures as more efficient masking should be taken to prevent the virulent organisms from contaminating the clean surgical wounds.

Airborne Pathogens.—The following measures should be taken outside the operating room: All infected persons should be isolated and as far removed from the operating room as possible. The infected patient should be discharged from hospital as soon as his general condition permits. After the infected patient's discharge from the hospital, his room should be thoroughly cleansed by suitable means. Portable ultraviolet lamps could be used to good advantage periodically during the patient's stay in hospital, as well as in the room after his discharge. Masks should be worn by the surgeon and all attendants when visiting or changing the dressings of such patients, in order to prevent contamination of their own nares as much as possible. Extra precautions should be taken in the sterilization of mattresses, blankets, and linen which have been exposed to septic wounds and dressings.

As for measures inside the operating room, the operating room is the last line of defense against wound contamination and by far the most important. If pathogenic organisms can be prevented from entering the operating room and contamination from within the operating room kept at a minimum, sepsis should be much less common.

The use of such measures as the constant passage of filtered bacteria-free air under pressure into operating rooms, arranged so that no other outside air could enter, would seem to be of some value in lessening a high infection rate, but they have not been as effective in eliminating wound infections as their originators hoped. Our studies would indicate that this is due to underestimation of the role of the operating room personnel in contaminating the operating room air, particularly via their nasal passages. The distance between the noses of the operating team and the wound is so short that it seems doubtful if any ventilating system can prevent bacteria from this source from gaining access to the wound. More effective measures to prevent the operating room personnel from bringing bacteria into the operating room are needed.

Summary and Conclusions

Under the usual sterile surgical conditions, the two most common sources of wound sepsis are nasal carriage of virulent staphylococci by members of the operating room team, particularly the surgeon or his immediate assistants, and airborne pathogens in the operating room. If the surgeon or his assistants are carriers, ordinary masks are not efficient enough to prevent transfer of these organisms from the nose to the wound, and under these circumstances an increased infection rate will occur.

If a surgeon finds that he has an epidemic of infections he should, first of all, consider his own nasal passages as the source and take measures to prove or disprove this. A special mask designed after the fashion of an airman's oxygen mask can effectively prevent this spread of virulent staphylococci from the nose of a nasal carrier to the surgical wound, with a resultant sharp decrease in the wound infection rate to a base-line level similar to that for bacteriologically innocuous personnel.

That airborne pathogens are of importance is indicated by the finding that the incidence of wound sepsis is significantly higher when such organisms can be demonstrated in the operating room air. These organisms themselves may, of course, originate from nasal carriers.

Operating room personnel should protect their nasal passages from contamination with virulent staphylococci by never attending patients with discharging wounds unless efficiently masked. Patients with discharging wounds should be isolated. The instruments used, the patient's skin, and the surgeon's cleansed hands must rarely cause wound sepsis. Ultraviolet light irradiation of an entire room for a few minutes has proved effective in clearing the air of its pathogens, and its use in this fashion between operations is recommended. More efficient masking of the operating room personnel and general measures to insure maximum bacteriological cleanliness of the air in the operating room would lead, in any institution, to a decrease in the surgical infection rate.

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NEWER PHENOTHIAZINE DRUGS IN TREATMENT OF NERVOUS DISORDERS

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The two most recent tranquilizing derivatives of phenothiazine are trifluoperazine (Stelazine) and thioridazine (Mellaril). The former is the most potent phenothiazine compound available. Its side-effects, predominantly extrapyramidal in nature, may be adequately controlled in the hospital, but the drug is not recommended for office patients unless given in very small doses. Thioridazine has about one-tenth the potency, weight for weight, of trifluoperazine but, in equivalent doses, is free of significant side-effects, including Parkinsonism. It is recommended for use in both the hospital and office.

It has been estimated that one-third of the practice of medicine is devoted to the treatment of nervous disorders, and it is a fact that one-half of the nation's hospital beds are devoted to this purpose. While chemotherapy is by no means the only treatment available to these patients, it is perhaps the one of greatest concern to the average physician. The past five years have seen the introduction of several new classes of drugs loosely referred to as tranquilizers or ataraxics. Some of these represent improvements over older classes of sedatives, as for instance meprobamate, which essentially acts like drugs of the barbiturate group. Others, and in particular the Rauwolfia alkaloids and the phenothiazine derivatives, display many entirely new pharmacological properties. Although most of these pharmacological effects are mediated through the central nervous system, they are utilized medically in the treatment of conditions that do not fall within the province of the neuropsychiatrist. They have indications in surgery and obstetrics as well as in the treatment of hypertension and intractable vomiting. However, much of the development of these compounds has taken place within the field of neuropsychiatry, and in its rapidity perhaps presents a confusing picture.

This paper deals with derivatives of phenothiazine, the compound with the now well-known three-ring structure containing one nitrogen and one sulfur atom (fig. 1). Though phenothiazine is toxic in itself, substitutions in the 2 and 10 positions have produced a remarkable series of drugs. One of the first of these, promethazine (Phenergan), was introduced as an antihistaminic, to be followed by diethazine (Diparcol), an anti-Parkinsonian agent, and the best known of all, chlorpromazine (Thorazine), which was actually first submitted (in the United States) as an antiemetic. All members of this family share the ability to sedate without impairing so-called higher cortical functions, i. e., to tranquilize. They also inhibit psychomotor activity to widely varying extents. In addition, they have more or less autonomic activity, antihistaminic

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effect, and local anesthetic properties. Further, some of them have pronounced effects on the extrapyramidal nervous system, including the reticular system and hypothalamic functions. Lastly, they are all more or less toxic, though as a rule the therapeutic index is surprisingly high. Research has progressed toward the aims of lesser toxicity, greater potency, and greater specificity of action.

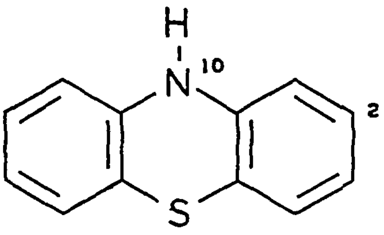

Fig. 1.—Structural formula of phenothiazine.

Greater potency of action so far as tranquilization is concerned has been achieved in two ways: first, by a change of halogen in the 2 position (fig. 2). For example, triflupromazine (Vesprin) is more powerful than chlorpromazine. Promazine (Sparine), which has no halogen in the 2 position, has about one-fourth the strength of chlorpromazine. The second way is by substituting a piperazine ring for the simple amino group in the side-chain on the 10 position (fig. 3). For example, prochlorperazine (Compazine) is at least five times as potent as chlorpromazine. A drug which incorporates both fluorine and piperazine substitution is trifluoperazine (Stelazine), and as might be expected this is the most potent phenothiazine derivative available at present. Unfortunately, nature does not bestow her favors without a price. Addition of both piperazine ring and fluorine moieties sharply increases the extrapyramidal effects. In the case of one experimental drug, SKF 6032, the most powerful phenothiazine yet tested, extrapyramidal effects were prohibitive. However, along with the increased extrapyramidal effect goes increased antiemetic power, which can be taken advantage of therapeutically, since drug-induced Parkinsonism usually requires a few days of dosage to develop to a significant degree. One major advantage of substituting a ring structure in the side-chain at the 10 position is the abolition of most of the adrenolytic and anticholinergic activity, e. g., there is little effect on blood pressure.

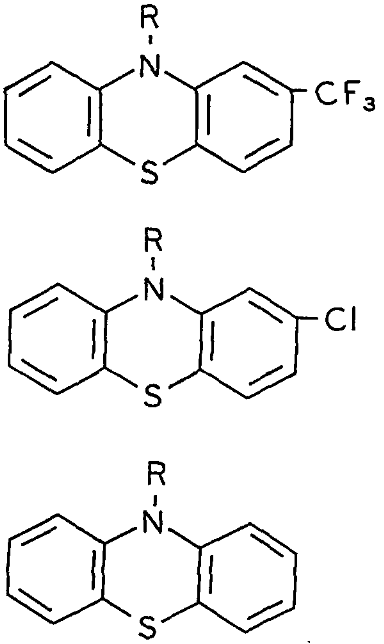

Fig. 2.—Structural formulas of (*top*) triflupromazine (Vesprin), (*center*) chlorpromazine (Thorazine), and (*bottom*) promazine (Sparine). (R = dimethylaminopropane.)

When a piperidine ring (one nitrogen atom instead of two) is used instead of the piperazine ring, *there is no increase in potency* but the compound appears to lose both its antiemetic and its extrapyramidal effects. One such drug, NP-207, tested some years ago, was found to be a highly effective tranquilizer but unfortunately exhibited a toxic effect on the retina. Replacement of the halogen atom at the 2 position by a sulfur-containing radical appears to have overcome the toxicity to the retina but retained the other desirable properties of NP-207. This compound is known as thioridazine

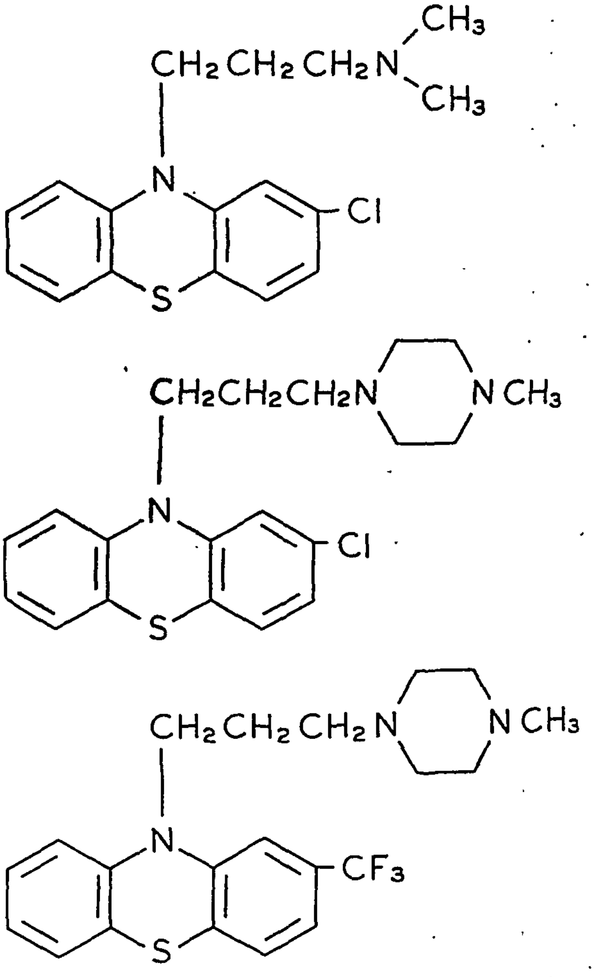

Fig. 3.—Structural formulas of (*top*) chlorpromazine, (*center*) prochlorperazine (Compazine), and (*bottom*) trifluoperazine (Stelazine).

(Mellaril) (fig. 4). The remainder of this paper will summarize work on my service with trifluoperazine (Stelazine)[1] and thioridazine (Mellaril).

Results with Trifluoperazine

A total of 152 patients were treated with trifluoperazine. Most were hospitalized for at least the beginning of therapy. Eighty were suffering from schizophrenia and were selected largely on a basis of failure to respond to other chemotherapeutic agents. Thirty others had been given a diagnosis of a variety of other psychotic disorders. The remaining 40 patients were given trifluoperazine as an aid in the management of excitement or restlessness, and these are not considered in detail or included in the tables.

The drug was given both parenterally and orally, though where possible oral medication was used. For calming very disturbed patients, one or more doses of 5 to 10 mg. intramuscularly proved very effective. For purposes of comparison, 50 to 100 mg. of chlorpromazine would have been necessary to achieve the same degree of sedation. For long-term treatment of schizophrenic patients, dosage was initiated at 5 mg. four times daily and increased by daily increments to an average of 80 mg. daily.

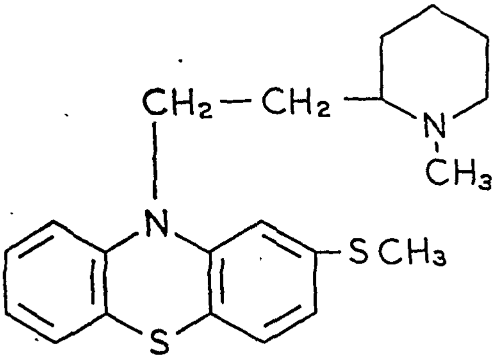

Fig. 4.—Structural formula of thioridazine (Mellaril).

As the study progressed, it became evident that dosage twice daily was sufficient to maintain adequate therapeutic effect. Average duration of intensive treatment was four weeks, though many patients continued on maintenance doses after discharge to the outpatient clinic or office. It was rarely necessary to interrupt treatment, since side-effects, when they occurred, could be controlled. A number of patients, however, discontinued medication after discharge from hospital, with subsequent relapse. The maximum duration of treatment was 18 months.

The results are summarized in tables 1 and 2. Since the response of a psychiatric patient to any given treatment is subject to influence by a number of variables, the method of reporting results has been simplified and based largely on social criteria. The improvements achieved are essentially comparable with those obtained on my service with other phenothiazine drugs. However, patient acceptability was good, injections were not painful, and side-effects were few except for the extrapyramidal symptoms. Orthostatic hypotension was complained of by a few patients but was not troublesome. Other signs of autonomic system disturbance were inconspicuous, though dryness of mouth and blurring of vision were noted. Two patients in the series exhibited a minor macular eruption which quickly subsided. There was no photosensitivity. Normal values were obtained for serial studies of hepatic function, blood cell counts, and urine analyses made during treatment on 29 patients.

Table 1.—*Results with Trifluoperazine in Eighty Schizophrenic Patients*[*]

Clinical Status	Sex	Very Satisfactory	Satisfactory	Unsatisfactory
	Nonintensive Treatment[†]			
Acute (8)	Male	..	5	..
	Female	..	2	1
Chronic (10)	Male	..	3	2
	Female	..	2	3
	Intensive Treatment[‡]			
Acute (25)	Male	4	1	4
	Female	9	4	3
Chronic (37)	Male	3	8	5[§]
	Female	1	10	10

[*] "Very satisfactory"—largely or completely symptom-free and able to return home or resume normal activities. "Satisfactory"—substantial relief; some able to return home and resume more or less normal exis[illegible] received little or no benefit or were worse.

[†] [illegible] not exceed 20 mg.

[‡] [illegible] osage 80 mg.

[§] One patient died.

Disturbance of the extrapyramidal system was seen in slightly over half the patients treated intensively. It occurred in two main forms. The typical syndrome of drug-induced Parkinsonism was noted in about three-quarters of the patients affected. Rigidity, shuffling gait, masking of the face, salivation, seborrhea, and occasional tremor were the main symptoms. The other form may be regarded as a kind of dystonia or torsion spasm. Sometimes it occurred along with Parkinsonism. Characterized by spasms of the neck muscles and shoulder girdle, on one or both sides, it developed gradually or paroxysmally. Occasionally there was spasticity of the entire trunk musculature and the tongue and other muscles of deglutition.

Table 2.—*Results with Trifluoperazine in Thirty-two Psychiatric Patients Other Than Schizophrenics*

Type of Disorder	Sex	Very Satisfactory	Satisfactory	Unsatisfactory
Depression (3)	Male	..	1	..
	Female	..	..	2
Mania (3)	Male	1	1	1
	Female	..	..	..
Delirium tremens (14)	Male	10	..	1
	Female	3	..	..
Chronic brain syndrome (9)	Male	..	2	3
	Female	..	3	1
Personality disorder (3)	Male	1	1	1
	Female	..	..	..

These phenomena are usually seen after 5 to 10 days of treatment but may occur sooner. Though dramatic, they are always reversible, either by reducing the dosage of the drug or by the simultaneous giving of anti-Parkinsonian agents. Of these, benztropine (Cogentin) methanesulfonate is the most effective. The one fatality in this series appeared to be related to sudden paralysis of brain stem function. The clinical picture in this case was that of acute encephalitis. Since all spinal fluid examinations for viruses were negative, it must be presumed that death resulted from massive brain stem inhibition caused by the drug.

It may be concluded, therefore, that trifluoperazine is about 10 times as potent milligram for milligram as chlorpromazine, measured in terms of tranquilizing capacity. It is a highly potent antiemetic agent. Average therapeutic doses cause extrapyramidal symptoms in one-half of the cases, though other side-effects are minor. It may be recommended for use with severely mentally ill hospitalized patients where intensive treatment is necessary and where extrapyramidal effects may be safely managed. Immediate withdrawal of the drug is advised whenever signs of brain stem inhibition appear.

Table 3.—*Data on Patients Treated with Thioridazine**

Type of Disorder	Condition	No. of Patients	Daily Dosage, Mg.			Duration of Treatment
			Maximum	Optimum	Maintenance	
Functional psychoses	Acute	41	2,000	1,200-1,600	200-600	1 mo. plus several months' maintenance
	Chronic active	53	2,400	1,200-1,600	300-800	6 wk. plus indefinite maintenance
	Chronic residual	24	2,400	2,000	300-800	6 wk. plus indefinite maintenance
	Ambulatory	23	1,600	600-1,300	300-600	Indefinite maintenance
Psychoneuroses	Acute	9	600	100-400	Not required	1-4 wk.
	Chronic	14	1,600	200-400	75-400	Indefinite maintenance
Psychosomatic reactions	Acute	2	400	100-400	Not required	1-4 wk.
	Chronic	7	1,600	200-400	75-300	Indefinite maintenance
Brain syndromes	Acute	10	1,200	800-1,200	Not required	2-10 days
	Chronic	15	1,600	200-1,200	150-600	Indefinite maintenance

* Age range: 13 to 77 yr.; males 78, females 120; ambulatory 48, hospitalized 150. Length of treatment: over 9 mo.

Results with Thioridazine

Thioridazine has been used in the treatment of 198 patients on my service during the nine months prior to writing. The series has included both ambulatory and hospitalized patients. In the case of inpatients, at least, selection was based where possible on failure to respond to previous chemotherapy with drugs of this type. In this way patients served as their own controls. A summary of the types of cases treated is given in table 3.

Dosage with thioridazine is essentially the same as that for chlorpromazine. Psychotic inpatients were started on therapy with 100 mg. four times daily by mouth, with daily increments up to a level at which a therapeutic response (measured by increased sociability, normalization of psychomotor behavior, and improved thinking) was obtained. The optimum dose has ranged from 1,200 to 1,600 mg. daily, depending largely on the chronicity of the illness. (Recent experience has suggested that somewhat lower dosage is adequate.) Therapy was kept at the optimal dose for 10 to 14 days, after which it was reduced to a maintenance dose. Patients were then usually discharged from the hospital and treated in the outpatient clinic or office. With all conditions except acute schizophrenia it was desirable to maintain treatment indefinitely. When this was done, relapse was much less frequent. This, of course, is true for all tranquilizing drugs.

Patients with minor mental disorders, psychoneuroses, and psychosomatic reactions were given much smaller doses of the drug primarily for the purpose of reducing tension and anxiety and related symptoms (table 3). Some were receiving psychotherapy in addition.

It should be noted that a form of thioridazine for parenteral use is not available, since the substance is unstable in solution. On this account it was necessary to treat a few of the very disturbed patients with some parenterally given preparation until they were able to take thioridazine tablets. A number of patients toward the end of the series were given long-acting tablets (Spacetabs) twice daily in place of the standard tablet. In general, it was found that these patients required about two-thirds of the total daily dose necessary with the standard tablet.

Results are shown in table 4 and again are simplified to avoid the pitfalls inherent in trying to measure precisely degrees of recovery from psychiatric illness. Patients in the "very satisfactory" category were largely or completely symptom-free and were able to return home or in the case of outpatients to resume their normal activities. "Satisfactory" responses include those who were afforded substantial relief and who were in many cases able to return home and resume a more or less normal existence. The last group received little or no benefit and in a few cases were worse. It is practically impossible to make adequate comparisons of one tranquilizing drug with another purely in terms of recovery rate. There is too great a variability in the criteria employed by different authors as well as in the method of presentation of results. Even on my own service, where many drugs of this type have been tested over the past five years, sometimes on the same patients, the task is not easy. Table 5 lists according to their responses to thioridazine the patients in several disease categories who had been previously treated with other tranquilizing drugs. These results are perhaps somewhat misleading in that the inclusion of a patient in this table does not necessarily mean that he completely failed to respond to the previous chemotherapy. Some of the patients had responded but had relapsed because of increased stress at home, failure to continue maintenance medication, or some other reason. The table does indicate that responses to thioridazine were usually quite satisfactory.

The most striking aspect of thioridazine therapy is the poverty of side-effects (table 6). As had been predicated from its chemical structure, extrapyramidal symptoms did not appear. Nor was there evidence of the increased tension and restlessness commonly seen with trifluoperazine and even chlorpromazine at the beginning of treatment, a symptom considered to be a "pre-Parkinsonian phenomenon" or indication of pharmacological stimulation of the extrapyramidal system. For this reason alone the drug was exceedingly well accepted by outpatients who often had become alarmed by these side-effects with previous medicaments. Though that aspect of thioridazine has not been investigated clinically, animal experiments suggest that it will be of no value as an antiemetic. The nature of the close relationship between extrapyramidal and antiemetic action is an elusive one, though pharmacological studies in animals indicate such a relationship.

TABLE 4.—*Results with Thioridazine in 198 Patients*

Diagnostic Category	No. of Cases	Very Satisfactory	Satisfactory	Unsatisfactory
Schizophrenia				
Acute	38	21	12	5
Chronic paranoid	32	7	16	9
Other	35	6	23	6
Residual	30	2	14	14
Brain syndrome				
Acute	10	9	1	..
Chronic	15	4	6	5
Psychoneurosis				
Acute	9	4	3	2
Chronic	10	..	5	5
Psychosomatic disorder				
Acute	2	1	..	1
Chronic	6	1	2	3
Depression	8	1	2	5
Mania	3	2	1	..

Drowsiness and lethargy did occur in some of the patients but was much less marked than with any other phenothiazine compound in equivalent dosage. With the exception of dryness of mouth, which was common, and orthostatic hypotension, which occurred in six patients, there were no side-effects attributable to disturbance of the autonomic system. Three patients developed transient edema, one of the face and two of the ankles. Two female patients experienced stimulation of the breast with some degree of lactation. This strange effect is occasionally seen with all the phenothiazine drugs and presumably represents a functional inhibition of the hypothalamic control of the pituitary gland.

There was no evidence of hepatic toxic effects. Thirty-four patients had repeated batteries of liver function tests during periods as long as 10 weeks, and blood analyses were performed concomitantly and consistently returned normal values. There was one case of mild dermatitis, but this could not be definitely attributed to the drug. Photosensitization did not occur.

TABLE 5.—*Results with Thioridazine in Patients Previously Treated with Other Tranquilizing Agents*

		% Classed with Result as			
Diagnostic Category	No. of Cases	Improved	Very Satisfactory	Satisfactory	Unsatisfactory
Schizophrenia					
Acute	18	89	61	28	11
Chronic paranoid	19	84.2	31.6	52.6	15.8
Other	23	73.9	21.7	52.2	26.1
Residual	21	56.1	9.5	47.6	42.9
Chronic brain syndrome	6	66.6	33.3	33.3	33.3
Chronic psychoneurosis	8	62.5	12.5	50	37.5
Chronic psychosomatic disorders	4	75	25	50	25

In conclusion it may be said that thioridazine is at least as effective in relieving psychiatric illness as other drugs of its class. On a milligram for milligram basis it has the same order of potency as chlorpromazine. In its low incidence of side-effects and toxicity it is superior to all other tranquilizing drugs tested. For this reason it is well tolerated by patients, particularly those who are not hospitalized and who frequently discontinue their medication with other drugs because of dizziness, sleepiness, increased tension, or Parkinsonism.

TABLE 6.—*Side-effects from Thioridazine in Patients Previously Treated with Other Tranquilizing Agents*

Side-effects	During Treatment with Thioridazine	During Treatment with Previously Administered Tranquilizing Drugs
Extrapyramidal symptoms	None	Very common
Lethargy and drowsiness	Rare	Very common
Orthostatic hypotension	Very rare	Occasional
Dryness of mouth	Common	Common
Dermatitis and photosensitivity	None	Occasional
Convulsions	None	Rare
Gastric irritation	Occasional	Occasional
Lactation	Rare	Rare
Edema	Very rare	Very rare
Blood dyscrasia	None	None
Hepatic dysfunction	None	None

Summary

The two most recent additions to the phenothiazine family of tranquilizing agents are trifluoperazine (Stelazine) and thioridazine (Mellaril). Trifluoperazine is the most potent phenothiazine compound available and has side-effects predominantly of an extrapyramidal nature. While these may be adequately controlled in the hospital, the

drug is not recommended for office patients, unless given in very small doses. Thioridazine has about one-tenth the potency, weight for weight, of trifluoperazine but in equivalent doses is free of significant side-effects, including Parkinsonism. It is recommended for use both in the hospital and in the office.

The trifluoperazine used in this study was supplied as Stelazine by Smith, Kline & French Laboratories, Philadelphia, and the thioridazine, as Mellaril by Sandoz Pharmaceuticals, Hanover, N. J.

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ANGIOCARDIOGRAPHIC STUDY OF ATRIAL THROMBI WITH SURGICAL-PATHOLOGICAL CORRELATION

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Because of the lethal potentialities of intracardiac thrombi in heart disease, the differential diagnosis between thrombi and intracardiac tumors can be lifesaving. The usual roentgenographic studies are not adequate for this purpose, but angiocardiography is frequently decisive. Its usefulness is illustrated by five case histories in which accurate diagnosis by angiocardiography led to successful surgical correction and was verified by the findings at operation and by the pathologist's report on findings in the excised portion of the auricular appendage. Twenty-six consecutive cases of rheumatic mitral stenosis were studied by this method with convincing results.

Important to the physician interested in surgery of the heart is knowledge of the presence and exact location of atrial mural thrombi, auricular myxomas, and other intracardiac tumors. The diagnosis of all these conditions is possible by modern angiocardiography.[1]

Patients coming to cardiac surgery, especially mitral valvulotomy, should have angiocardiography. Angiocardiography can demonstrate atrial thrombi. This diagnostic method should be performed before peripheral arterial embolectomy and general surgical procedures on the chest and upper part of the abdomen of patients with known rheumatic valvular disease, especially those with auricular fibrillation. Because the embolization during operation or in the postoperative period is a grave occurrence, the presence or absence of atrial thrombi ought to be determined.

Peripheral arterial embolism is responsible for the death of more than 20% of patients who die of rheumatic heart disease. In other patients, emboli may cause serious and permanent disability. Experience has shown that angiocardiography is the most helpful single test for a correct clinical diagnosis of intracardiac thrombi. A confirmed diagnosis is invaluable for use of prophylactic anticoagulant therapy or for preparation for technical performance of the operation by the surgeon. An early and accurate diagnosis of auricular thrombi can actually represent a lifesaving measure and is, in itself, an indication for operation.

Pulmonary infarction is often assumed to come from phlebothrombosis in the absence of local signs. Unless angiocardiography is used, it may not be possible in such an instance to determine if the source is not the right atrium. If right auricular thrombi are not demonstrated, then the peripheral veins are the usual source of the emboli.

In rheumatic heart disease, the left atrium and its appendage are the most common sites of intracardiac thrombosis. Less frequently, the right atrium and its appendage are sites of thrombus formation. Thrombi are rarely present in the ventricles. Intracardiac thrombi have also been reported with myocardial infarction, hypertensive heart disease, bacterial endocarditis, endocardial fibroelastosis, amyloidosis, and rarely with subendothelial hemorrhage. Atrial thrombi associated with mitral stenosis is the subject of this report.

The incidence of intracardiac thrombi has been estimated from 5.3 to 7.9%.[2] Certain factors in-

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crease the incidence. In the study by Wallach and his associates,[2a] thrombi were found in at least one or more of the cardiac chambers of patients with rheumatic heart disease. These authors reported an incidence of 26.9% among 8,676 autopsy studies. In 106 patients with severe rheumatic mitral stenosis, thrombi in the left atrium and/or the appendage were found associated with thrombi in other chambers of the heart. This is commonest when auricular fibrillation is present.[3] The greater degree of stenosis of the mitral valve, the more common are atrial thrombi. Harvey and Levine [2b] found the most common site of thrombus formation in heart diseases of all types to be right auricle and the apex of the left ventricle. A sex difference was apparent; males have thrombi twice as often as females. The incidence of coronary artery disease in males is greater and may account for this finding.

Soloff and Zatuchni [1a] reported on 57 patients with rheumatic heart disease. They recognized mural thrombi, exclusive of thrombi present only in the left atrial appendage, in 8.8% of the patients. This finding compares favorably with postmortem observations of patients with mitral stenosis. Zinsser and Johnson [4] called attention to the value of angiocardiography in demonstrating auricular thrombi, but they did not study the matter further. Although Steinberg [5] recently reported in one paper that thrombi do not produce opacification defects in the left atrium, he must be given credit for first pointing out that one can visualize atrial thrombi by angiocardiography.

Antemortem formation of mural thrombi within chambers of the heart is not an uncommon occurrence. These thrombi are important not only as a source of peripheral emboli but, on occasion, by occlusion of the outflow of blood from the atrium, as a cause of decreased cardiac output. These occlusive auricular thrombi have been the subject of many reports and are of three types: ball thrombus, pedunculated thrombus, and mass thrombus. The incidence of occlusive auricular thrombi found on routine postmortem examinations has been variously reported to range from one in every 540 to one in every 3,000 autopsies. Several studies place the incidence of ball thrombus as approximately one in every 2,000 autopsies.

The occurrence of ball thrombi in patients with rheumatic heart disease is more frequent. Garvin reports one in every 52 subjects, and Wallach found a ball thrombus in one in every 32 autopsies on rheumatic heart disease. Evans and Benson [6] report the highest incidence of occlusive auricular thrombi, one in every eight patients coming to autopsy from mitral stenosis.

Since the first description in 1814 by Wood, there has been a growing interest in the dramatic clinical symptoms produced by occlusive thrombi, and because the diagnosis may be confirmed in vivo by angiocardiographic means, a greater interest in the use of this method should be stimulated. The clinical diagnosis has been helpful in but a few patients. The first successful antemortem clinical diagnosis was made by Bozzolo [7] in 1896.

Atrial thrombi may occur in other types of heart disease: hypertensive heart disease,[8] rheumatic heart disease, acute vegetative endocarditis, coronary sclerosis, thromboangiitis obliterans, and atrial infarction.[9] Reports on the clinical and pathological features of ball valve and other types of occlusive thrombi of the left and right atrium have been published.[8b] All fail to emphasize the value of angiocardiography as a possible means of diagnosis. Reports of intracardiac thrombi have usually been on autopsy material. Angiocardiography is the sole method by which thrombi can be demonstrated in the living patient.

Value and Limitations of Roentgenologic Study

The presence of intracardiac auricular thrombi cannot be demonstrated by the usual roentgenographic techniques. Massive atrial thrombi may produce very dense shadows within the cardiac shadow or an abnormal cardiac silhouette.[10] Arendt noted an unusual prominence of the left auricular appendage on the straight left cardiac border as suggestive of atrial mural thrombus formation. Other roentgenologic signs have been used for the diagnosis of left atrial thrombosis but are unreliable. Diminished pulsations of the auricles are of no value. Calcified thrombi may be visible within the left atrium, but this is rare. Calcification of the posterior wall of the left atrium may suggest an overlying thrombus, but thrombi are commonly present without calcification. Small areas of calcification in the region of the atrial appendage have been reported as due to small thrombi.[11] Large thrombi in the left atrium may appear as extensive shell calcification. These signs are inconclusive and may represent other conditions.

Value and Limitations of Angiocardiography

Abnormal masses within the atria are exhibited by persistent defects of opacification on angiocardiography. Areas with poor or no opacification of the atrial chambers provide evidence for thrombi. The Robb-Steinberg technique of angiocardiography was used with the Sanchez-Perez angiocardiographic apparatus. Three doses of opaque medium were used for a complete study. (Either 70% sodium acetrizoate [Urokon sodium] or 90% diatrizoate [Hypaque] sodium was used in doses of 50 to 60 cc. for each study.) Studies in the posteroanterior and left anterior oblique position were made for each patient.

In patients without valvular disease the angiocardiograms were characterized by the free passage of opaque material from one chamber to the next in a normal sequence beginning with the right atrium and progressing rapidly through the other chambers. With a normal circulation time the entire right heart and lesser circulation were maximally opacified within two seconds and usually faded by six seconds.[4] The left side of the heart began to show opacification within 4 or 5 seconds, with maximum opacification at 8 to 10 seconds. It was free of opaque material within 12 seconds or less after injection. The left side of the heart was completely opacified as a unit.

The variations from the normal in structural outline and hemodynamics are observed. Areas of nonopacification in the atria point to an intracavitary abnormality.

Criteria have been established relative to the appearance of the cardiac chambers and the great vessels in acquired valvular disease.[5] Diagnosis of valvular heart disease in obscure cases with absent or doubtful murmurs may be helped by angiocardiography. The selection of patients for valvulotomy is aided by the procedure.

Relationship of Angiocardiographic Diagnosis of Auricular Thrombi and Surgical and Pathological Findings in Twenty-six Consecutive Patients

	Findings		
No. of Case	Angiocardiographic	Surgical	Pathological
1	−	−	−
2	−	−	−
3	−	−	−
4	−	−	−
5	−	...†	...†
6	+	−	−
7	−	−	−
8	−	−	−
9	−	−	−
10	+	+	−
11	−	−	−
12	−	...‡	...‡
13	−	−	−
14	−	−	−
15	+	−	+
16	+	−	+
17	+	−	+
18	+	+	+
19	−	−	−
20	+	+	+
21	−	−	−
22	−	−	−
23	+	−	+
24	+	+	+
25	+	+	+
26	...*	−	+

* Both atria contained thrombi. Right atrial thrombus was visualized by angiocardiography, but surgeons failed to explore chamber; thus it was not confirmed. Left auricular thrombus was confirmed by pathological examination but failed to be noted at time of operation.

† Pericardiectomy performed for constrictive pericarditis.

‡ No operation performed.

In the normal subject the atrium has a homogeneous appearance. In patients with mitral stenosis or with conditions with an increased end diastolic pressure in the left ventricle, the left atrium becomes enlarged, sometimes markedly, and spherical in shape. In patients with mitral stenosis, a barrier to the free passage of blood between the left atrium and ventricle is present. Opacification of the left atrium is intense and homogeneous and persists for a longer period of time than in the normal atrium. Visualization of an intra-atrial mass is likely.

Left atrial thrombi produce areas of nonopacification which persist throughout serial films. These defects in opacification have irregular margins and are not sharply demarcated. The atrial chamber border is indefinite. When thrombi are present in the auricle, opacification does not occur or is most irregular. Mural thrombi of the right atrium give identical angiographic appearances. Myxomas usually have sharp margins about the area of nonopacification; a ball valve thrombus may look the same. Myxomas are distinguished by their attachment, not to the posterior wall of the left atrium but to the atrial septal wall in the region of the fossa ovalis. Thrombi may be attached to any wall but usually to the posterior atrial wall. It is rare for mural thrombi to be as large as myxomas.

A turbulent stream of regurgitant blood flowing through an incompetent mitral valve may create difficulty for diagnosis. But the inconstancy of the heterogeneous opacification on serial films is the clue. Diagnosis of thrombus of the left atrium is a more difficult problem than for the right atrium. The opaque medium becomes diluted on passage through the pulmonary bed. Dilution is greater the more prolonged the circulation time. This difficulty is avoided by use of sufficient opaque medium with rapid introduction.

Diagnosis of left auricular thrombosis is made only when irregular areas of nonopacification persist on serial films. These areas are irregular in shape and have unclear margins. These angiocardiographic criteria are stated by Soloff and Zatuchni.[1a]

Studies of 26 consecutive patients form the basis of this report. The interpretation of the angiocardiographic, surgical, and pathological findings were recorded independently (see table). All patients studied had rheumatic heart disease with mitral stenosis. Only one angiocardiographic study (case 16) was doubtful. Of the 10 patients found to have atrial thrombi, there was no confirmation in 2, either by surgery or at autopsy. In the remainder there was confirmation at operation or by pathological examination. Autopsy studies in six patients confirmed the presence of atrial thrombi. Confirmation of the angiocardiographic diagnosis was supported better by the pathological examination than by the surgical findings. The assessment of the presence or absence of auricular thrombi is difficult for the surgeon. This difficulty may lessen when open-heart surgery is used for all valvular lesions. The over-all incidence of atrial thrombi in this group of patients is 36%. This compares favorably with the expected incidence reported from postmortem studies. Four illustrative case reports are presented.

Report of Cases

CASE 15.—A 58-year-old woman entered Kings County Hospital Center with the chief complaint of shortness of breath. Ten months before admission, dyspnea on exertion, orthopnea, ankle edema, and palpitation had developed. An attack of chorea (St. Vitus dance) had occurred when the patient was aged 12. On physical examination, the blood pressure was 120/80 mm. Hg, the pulse rate was 79 per minute, and atrial fibrillation was present. An apical systolic and late diastolic murmur were present. A systolic murmur was heard to the right of the xiphoid. The apical impulse was 3 cm. to the left of the midclavicular line in the fifth intercostal space. The radiographs of the chest showed slight straightening of the left cardiac border and an increase in the cardiothoracic ratio. The barium swallow was normal. A phonocardiographic study recorded the Q-1 interval at 0.07 to 0.08 seconds and the Q-2 interval at 0.33 seconds. The first mitral sound was loud. Neither an opening snap nor an apical diastolic murmur was recorded on this study. At Erb's point, the first sound was preceded by a low pitched, short, soft, diastolic rumble. A jugular phlebogram revealed a relatively large "C" wave, indicating tricuspid insufficiency. A study by slit-kymogram indicated a large heart with normal filling and emptying curves. Catheterization studies confirmed the tricuspid insufficiency.

On this study, pulmonary hypertension was noted. A giant right atrium and an enlarged right ventricle were demonstrated by angiocardiography. The inferior vena cava was seen to be dilated. The major pulmonary arteries were dilated but abruptly narrowed after the secondary branches. At 22 seconds the left atrium was densely opacified while the left ventricle was poorly opacified. The left auricular appendage never became opacified. This study was interpreted as indicating the presence of mitral stenosis, tricuspid stenosis, left auricular thrombosis, and marked pulmonary hypertension (fig. 1 *A* and *B*). At operation, no thrombus was palpated. A mild degree of regurgitation was noted. A finger fracture was done, and the left auricular appendage was amputated. Postoperatively, the patient was improved. However, no change of the Q-1 interval occurred. The first mitral sound was still loud, and the opening snap was still absent. Infiltration of the pericardium and interstitial portion of the muscle with chronic inflammatory cells was reported by the pathologist. Endocardial fibrosis with organizing thrombosis were additional findings. Aschoff bodies were not found. The diagnosis was pancarditis, suggestive of active rheumatic fever and thrombosis of the atrial appendage.

CASE 18.—A 63-year-old woman entered Kings County Hospital Center after embolism of the right common femoral artery. For 20 years palpitations had been a complaint. Hemoptysis and congestive heart failure had occurred four years ago. Auricular fibrillation was present then. A history of rheumatic fever was not elicited. On physical examination, auricular fibrillation and cardiac enlargement were found. The radiographs of the chest showed an increase in the transverse diameter of the heart without a mitral configuration.

On phonocardiographic study, the Q-1 interval was found to be 0.06 seconds and the Q-2 intervals, 0.34 seconds. The time interval from the second sound to the opening snap was 0.06 to 0.08 seconds.

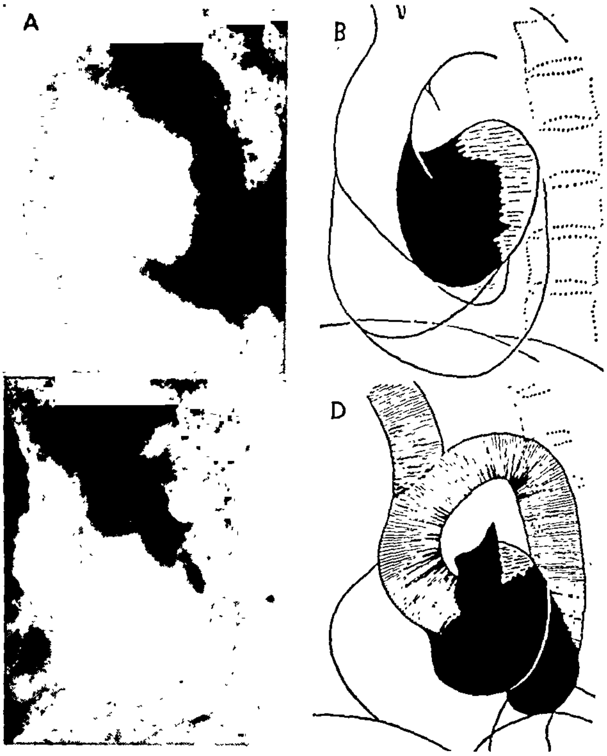

Fig. 1.—*A* (case 15), left anterior oblique angiocardiogram demonstrating constant filling defect extending from posterior wall of left atrium. Finding is definite for atrial thrombi. *B* (case 15), diagram of angiocardiographic findings, to show extent and location of thrombus in left atrium. *C* (case 18), left anterior oblique angiocardiogram showing nonopacification high on posterior wall of left atrium. Filling defect, noted on several films, is definite evidence for atrial thrombi. *D* (case 18), diagram of angiocardiographic findings.

The first sound at the apex was loud and split. A high-pitched systolic murmur over the whole precordium was recorded. A low pitched diastolic rumble was picked up both at the apex and at Erb's point. The pulmonic second sound was accentuated. A slit-kymograph showed both ejection and filling phases to be rapid. The left anterior oblique view of the angiocardiographic study showed an area of nonopacification, irregular in contour, on the posterior wall of the left atrium (fig. 1 *C* and *D*). This was interpreted as a left atrial thrombus in the presence of mitral stenosis.

At operation the left atrial appendage was found reduced in size. A clot was found at exploration with the finger. A regurgitant jet was not noted. The mitral orifice was "tight" but fractured easily. The pathologist reported the presence of clusters of chronic inflammatory cells in all layers of the auricular wall, but definite Aschoff bodies were absent. Zones of fibrosis were also noted. Inactive rheumatic carditis with organized thrombus was the interpretation.

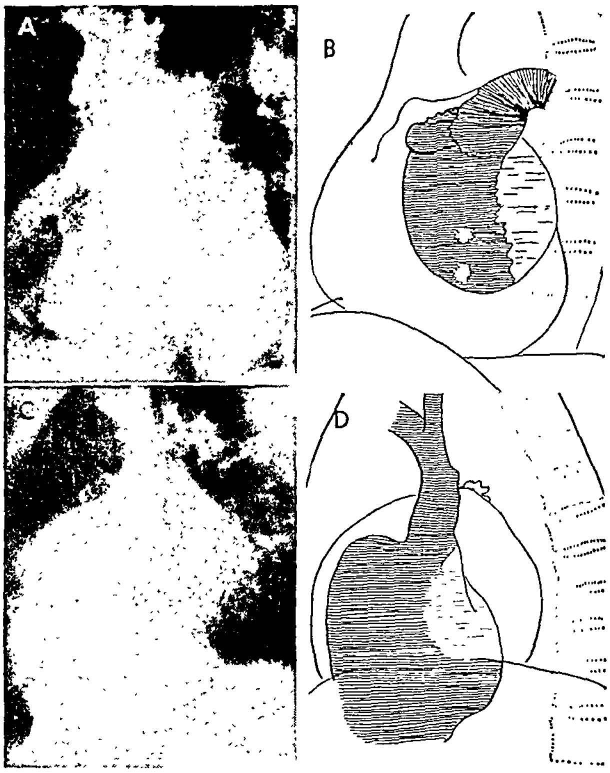

Fig. 2.—*A* (case 20), left anterior oblique angiocardiogram showing constant filling defect in left atrium along posterior wall and two smaller areas of nonopacification within body of atrium. *B* (case 20), sketch of angiocardiographic findings showing areas of nonopacification in left atrium. *C* (case 26), right lateral angiocardiogram showing early opacification and persistent area of nonopacification of posterior wall of right atrium. This is characteristic of right atrial thrombus, and its attachment distinguishes it from right atrial myxoma. This is shown to indicate appearance of thrombus in right atrium which is less frequent than occurrence in left atrium. *D* (case 26), diagrammatic representation showing extent and location of right atrial thrombus.

Case 20.—A 45-year-old man was admitted to the medical wards of Kings County Hospital Center because of dyspnea of moderate severity. Congestive heart failure had been present for five and one-half years. Auricular fibrillation had been present for the past two years. A history of rheumatic fever was not elicited. On physical examination the apex impulse was found in the fifth intercostal space, 2 cm. to the left of the midclavicular line. A chest x-ray examination disclosed an increase of the transverse diameter of the heart, a straight left border, and no apparent valvular calcification. An esophogram was normal. The clinical diagnosis was rheumatic heart disease with predominant mitral stenosis. The angiocardiographic study was striking for a constant lack of opacification of the posterior left atrium on all the serial films. Two small areas of nonopacification in the inferior part of the atrium were also noted (fig. 2 *A* and *B*).

At operation the left atrium was felt to be packed with clot, but none was found in the atrial appendage. A regurgitant jet was not felt. A finger fracture of the mitral valve was successful. A postcommissurotomy syndrome occurred postoperatively. The pathologist reported hypertrophied atrial wall with organized mural thrombi for the atrial appendage specimen.

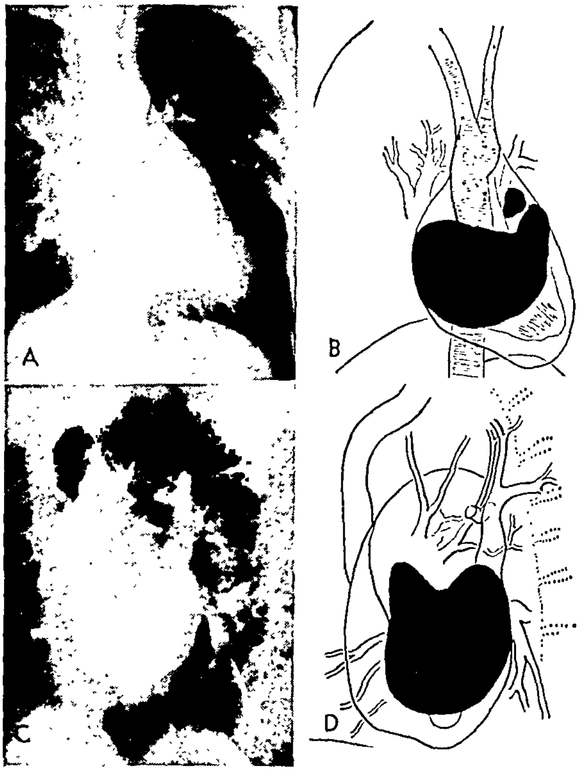

Fig. 3 (case 22).—Posteroanterior angiocardiogram showing dilated atrial chamber. Serial films showed retention of opaque medium. Note homogeneity of opacification of left atrium, indicating no atrial thrombi. Left auricle is easily identified. *B*, diagram showing homogeneity and contour of left atrium and auricle. Dilated pulmonary vein is sketched superior to left auricle. *C*, left anterior oblique angiocardiogram showing enlarged spherical left atrium and homogeneous opacification. This is characteristic angiocardiographic finding for mitrial stenosis without atrial thrombi. *D*, diagram of left anterior oblique angiocardiographic finding demonstrating homogeneous opacification of left atrium.

Case 22.—A 53-year-old woman entered Kings County Hospital Center with the chief complaint of shortness of breath. Congestive heart failure had been present for at least one year. Auricular fibrillation had been noted for the past nine months. A history of rheumatic fever was not recorded. On physical examination the heart was found to be enlarged to the left anterior axillary line. Roentgenograms of the chest showed cardiac enlargement, with a straight left ventricular border. The pulmonary artery segment was prominent. A suggestive double contour of the right cardiac border was seen. Valvular calcification was not present. The esophogram was normal. The clinical diagnosis was rheumatic heart disease with predominant mitral stenosis.

The electrocardiographic record showed auricular fibrillation. The ventricular rate was 100 per minute. Right axis deviation was present. The phonocardiogram recorded a loud delayed apical first sound, beginning 0.08 seconds after the Q wave of the electrocardiogram. The second sound began 0.36 seconds after the beginning of the Q wave. Apical murmurs were not recorded. At Erb's point, a definite opening snap was recorded which followed the second sound by 0.06 to 0.07 seconds.

The left ventricle showed prompt emptying but very slow filling on the slit-kymographic study. Small complexes and the absence of gallop waves were noted on the ballistocardiograph. The angiocardiographic study showed the characteristic findings of mitral stenosis, retention of the opaque medium in an enlarged spherical left atrial chamber with homogeneity of opacification. This study was interpreted as mitral stenosis without atrial thrombi. Patients with mitral stenosis without thrombi presented this angiocardiographic appearance (fig. 3). The presence of a severe mitral stenosis without insufficiency is characterized by these findings.

At operation a clot was not found. A minimal degree of regurgitation was noted, and a finger fracture of the mitral valve was done. Marked clinical improvement was noted postoperatively. The pathological diagnosis was reported as normal auricular appendage.

Case 26.—In 1957 a 67-year-old man had an embolus to the right leg and was admitted to the Kings County Hospital Center. Atrial fibrillation had been present since 1935. A dilated superior vena cava and an enlarged right atrium and right ventricle were demonstrated by angiocardiography (fig. 2 *C* and *D*). A persistent filling defect of the posterior wall of the right atrium was noted. The left atrial appendage was not visualized. The left atrium was of giant size and its opacification was prolonged and intense. Relatively little opacification of the left ventricle occurred. These findings were interpreted as indicating the presence of mitral stenosis with left auricular thrombosis and right atrial thrombus. At operation, a large thrombus was found in the left atrium. The right atrium was not explored. The pathologist stated that hypertrophy of the left auricular heart muscle was present. A minimal infiltration of chronic inflammatory cells of the cardiac muscle was also present. An organizing thrombus of the left atrium was also noted.

Summary

Angiocardiography is of value for the demonstration of intra-atrial thrombi. Twenty-six consecutive cases of rheumatic mitral stenosis were studied by this method. A diagnosis of intra-atrial thrombi made by angiocardiography was confirmed by the pathological study rather than the operative findings. There are several reasons for this discrepancy. Knowledge of the presence of atrial thrombi is important for prognosis and as an indication for mitral valvulotomy, in the absence of another indication for surgery.

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LEIOMYOSARCOMA OF THE UTERUS WITH UNUSUAL METASTASES

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It appears possible that recurrence of leiomyosarcoma may develop many years after presumably complete excision of the primary tumor. In this patient, metastases became symptomatic 18 years after total hysterectomy. It is the fifth case reported in the literature of metastases in a long bone and the second with retro-orbital metastases. One kidney was also extensively involved.

Sarcoma of the uterus was first reported by Mayer in 1860; Virchow made the pathological studies in this case. Many theories have been advanced to explain the etiology of uterine sarcoma. At present most authorities believe that tumors may arise from any of the cells present in an organ. Leiomyosarcoma of the uterus is believed to originate from smooth muscle cells either in the uterus or in pre-existing myomas.[1]

This unusual case is presented because either metastases or the development of a second sarcoma occurred 18 years after the patient had a total hysterectomy with complete removal of the primary tumor. This case is also unusual because metastases occurred in the upper part of the femur and the retro-orbital region. Retroperitoneal metastases involving the left kidney were present. When a leiomyosarcoma extends beyond the uterus there is usually fairly widespread local invasion into contiguous structures including the adnexa, urinary bladder, small intestine, and rectum. Distant metastases occur through hematogenous and lymphatic pathways. These most commonly involve the lungs, pleura, liver, intestines, omentum, kidneys, and brain.[2] Bone involvement, except for vertebrae and ribs, is rare.

Report of a Case

A well-developed, obese, 32-year-old woman was first seen at Henry Ford Hospital on May 6, 1937. She complained of lower abdominal pain and a sense of heaviness in the pelvis. Five pregnancies had resulted in three living children. There was no disorder of menstrual function. A large, firm, freely movable mass of irregular contour was present in the pelvis and extended 2 cm. above the umbilicus.

On May 12, 1937, with the patient under ether and ethylene anesthesia, a complete hysterectomy, left salpingo-oophorectomy, and appendectomy were performed. Attached to one cornu of the uterus was a large tumor mass which had a vascular surface and measured 18 cm. in diameter. At operation the tumor was not adherent to surrounding structures.

The cut surface of the tumor showed many foci of hemorrhage. The uterine canal appeared normal. Microscopic examination (fig. 1) showed the richly cellular tumor to be composed of interlacing bundles of spindle-shaped cells with large vesicular nuclei. An average of one mitotic figure per high-power field was seen. The central portion of the tumor showed extensive necrosis. The pathological diagnosis was leiomyosarcoma of a low degree of malignancy. Two weeks after operation the patient received deep x-ray therapy consisting of a daily skin dose of 720 r to the pelvis on four successive days. Convalescence was without incident and the patient remained well for the next several years.

In 1950, at another hospital, she had a thyroidectomy for a nontoxic colloid goiter. She continued in good health until July, 1955, when she began to limp because of moderate pain in the left thigh. The pain gradually became more severe, and walking became impossible. On Feb. 18, 1956, she came to the emergency room where roentgenologic studies (fig. 2A) disclosed a pathological fracture of the left femur just below the trochanters with an osteolytic zone at the fracture site.

On admission on Feb. 18, 1956, the patient was a well-developed, obese woman in no acute distress. Temperature was 99.8 F, (37.6 C) pulse 80 per minute, blood pressure 220/125 mm. Hg, and respirations 20 per minute. Dental caries was evident. There was normal sinus rhythm and slight cardiac enlargement, and a mitral murmur was detected. A hard mass descended 14 cm. below the left costal border with inspiration. There was considerable tenderness to palpation over the left femur at the junction of the upper and middle thirds. Flexion was impossible because of pain. Femoral pulsations were present with good peripheral circulation. Uterus and cervix were absent.

The hemoglobin level was 14 Gm. per 100 ml., and white blood cell count was 7,950 per cubic millimeter with 71% neutrophils, 4% eosinophils, 24% lymphocytes, and 1% monocytes. Specific gravity of the urine was 1.02 and reaction was acid. There was no sugar, but there was a trace of albumin. Results of microscopic examination were negative. The blood sugar level was 144 mg. per 100 ml., non-protein nitrogen level, 38 mg. per

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100 ml., and basic phosphatase level, 2.8 Bodansky units per 100 ml. Result of Venereal Disease Research Laboratories test was negative.

Table-top x-ray of the chest showed no abnormality of the lungs, though the heart appeared somewhat enlarged in the supine position. Metastatic survey demonstrated a large dense soft tissue mass in the left side of the abdomen and the osteolytic lesion of the femur previously noted. Intravenous pyelograms (fig. 2*B*) were made. There was a large mass involving the left kidney with deformity of the collecting system. The right kidney was normal. In roentgenologic studies of the upper gastrointestinal tract a mass 20 by 17 cm. was seen in the left side of the abdomen, causing a pressure defect on the greater curvature of the stomach. There was no calcification within the mass and the borders were smooth. The esophagus, stomach, and upper part of the small intestine were normal.

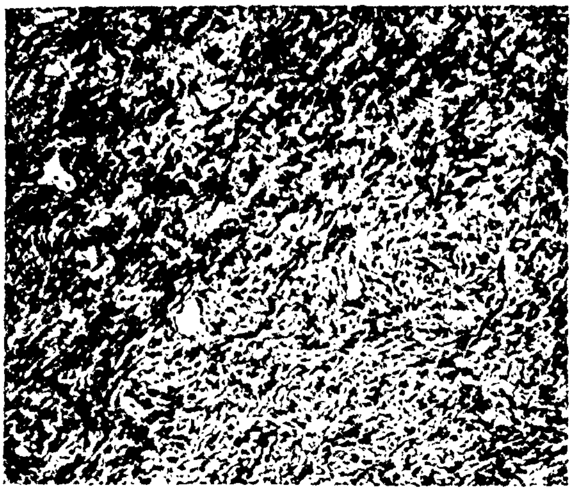

Fig. 1.—Photomicrograph of section from uterus, taken after hysterectomy in 1937. Richly cellular tumor is composed of spindle-shaped cells.

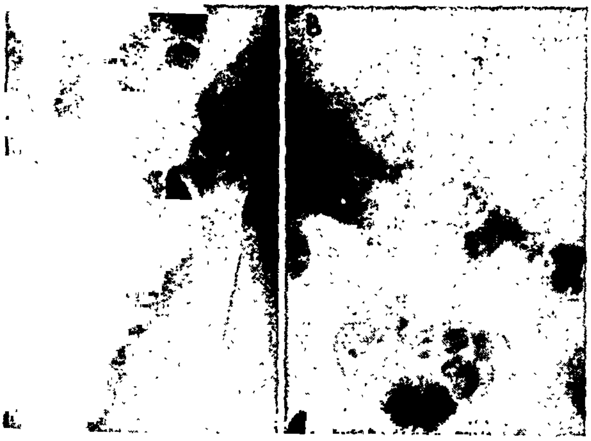

Fig. 2.—*A*, anteroposterior view, showing osteolytic lesion of upper shaft of femur with linear fracture. *B*, intravenous pyelogram, showing mass in left retroperitoneal region involving left kidney and producing deformity of collecting system.

On March 2, 1956, with the patient under endotracheal anesthesia, a specimen of the left kidney was obtained for biopsy through a left flank incision. An extensive tumor mass 35 cm. at its longest axis was found in the left retroperitoneal region. There were numerous firm nodules over the upper surface of the exposed left kidney. Microscopic examination (fig. 3*A*) revealed a tumor of interlacing bundles of elongated spindle-shaped cells similar to the uterine tumor removed in 1937.

After the patient recuperated from the above procedure open reduction of the femur was performed. As the incision was made through the sheath of the rectus lateralis muscle, light gray, soft, friable tumor tissue was exposed. This was curetted out and the fracture was immobilized with a Smith-Peterson nail and Thornton plate.[2A]

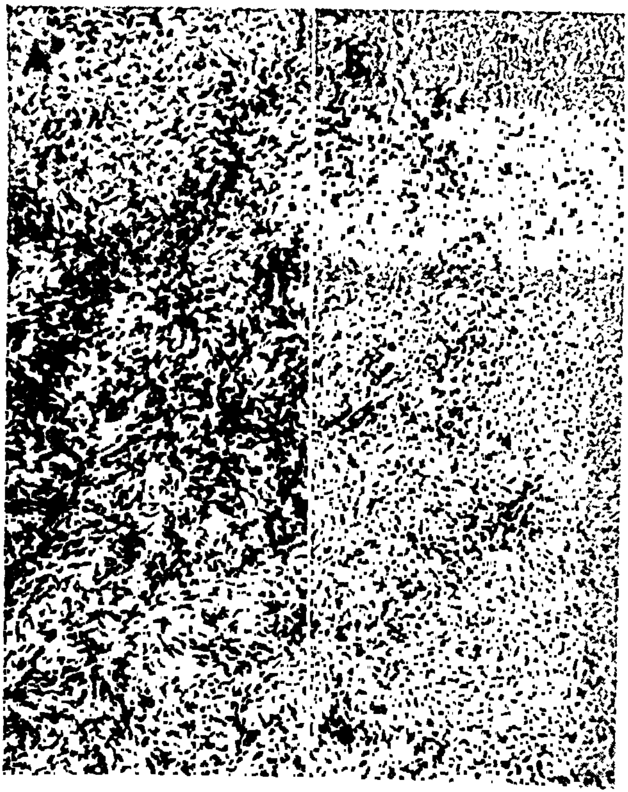

Fig. 3.—*A*, section from left kidney, obtained in 1956, showing interlacing bundles of elongated spindle-shaped cells. *B*, section from left femur.

Microscopic sections of the curetted material (fig. 3*B*) showed a vascular tumor invading and destroying bone and showing large areas of necrosis. It resembled the tumors previously removed from the kidney and uterus. The operative wound healed promptly and the patient left the hospital with a hip that was painless on gentle limited motion. Progress x-rays showed good healing although there was some bending of the Smith-

Peterson nail. She was allowed partial weight-bearing four months after reduction. The abdominal mass continued to grow.

In December, 1957, the patient noticed that her right eye was bulging outward, and vision became impaired. She experienced a "sticking sensation" and noticed redness of the eye. On examination on Jan. 16, 1957, the right eye was noncompressible. There was subconjunctival hemorrhage with limitation of the ocular movements in all directions. The eye was proptosed, although the lids covered the cornea when closed. There was redness and induration of the upper lid. Pupils were equal in size and reacted to light. Roentgenologic studies of the optic foramens showed evidence of soft tissue density of the right orbit. There was no evidence of bone involvement. Hydrocortisone acetate (Neo-cortef) was used locally to reduce the inflammation. By March, 1957, an extreme chemosis had developed. Although disfiguring (fig. 4) the eye condition was painless. Because of increasing proptosis enucleation was elected.

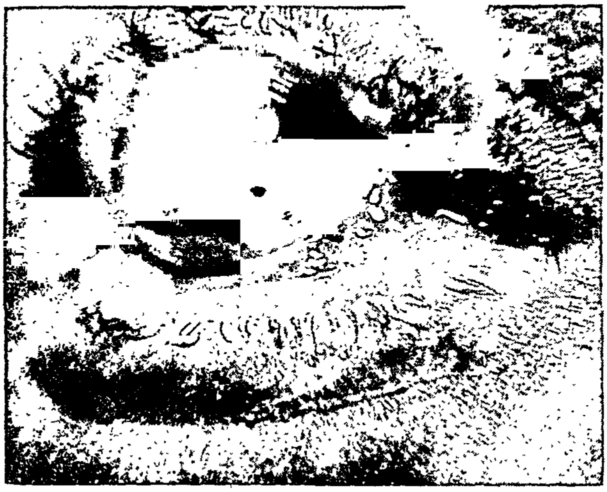

Fig. 4.—Photograph of right eye, showing proptosis and chemosis produced by retro-orbital metastatic leiomyosarcoma.

On March 19, 1957, with the patient under anesthesia with thiopental (Pentothal) sodium the right eye was enucleated and partial right orbital exenteration was performed. Tenon's capsule and the conjunctiva were closed with interrupted catgut sutures. The retro-orbital tumor measured 3 by 3 by 5 cm. and was grayish-white, soft, and rubbery. Microscopic sections (fig. 5) showed the tumor to be similar to those which had occurred in the uterus, kidney, and femur. No tumor was found in the eye. Edema subsided and the patient was referred for a prosthesis. There was no recurrence of tumor at this site.

In June, 1957, she had a good range of painless motion of the hip. The abdominal tumor continued to grow. There was edema of both legs, probably from pressure of the tumor on the inferior vena cava. Considerable bone formation had occurred at the fracture site over the intervening months. Som separation of the Smith-Peterson nail and Thornto plate had occurred. On July 6, 1957, while walkin with crutches, she felt sudden pain and a snappin sensation at the fracture site. Complete separatio of the Smith-Peterson nail and Thornton plate wa shown by x-ray, with motion demonstrable at th fracture site.

On July 11, 1957, with the patient under genera anesthesia, the Thornton plate was rebolted to th Smith-Peterson nail with good stabilization of th hip. A wound hematoma prolonged the postoperative course. Chest x-ray revealed a 2 cm. circula density in the left lung (fig. 6*A*), which was considered a metastasis. During the last week of Jul and first part of August, 1957, the patient received 5,000 tumor r in 20 treatments with radioactive cobalt (Co^{60}) teletherapy, at a tumor-sourc distance of 75 cm., using three 20.6 cm. round field about the abdomen. The femur received 5,00 tumor r with Co^{60} teletherapy in 20 treatment through opposed 10 by 10 cm. fields.

On Feb. 27, 1958, she was feeling well and he appetite was good. She had lost no weight. Ther was considerable new bone formation present. Sh experienced no pain on partial weight-bearing. On May 26, 1958, she reported some difficulty in breathing at night which was probably due to the massive tumor. Otherwise she was getting along well, even to the point of driving her car. Con-

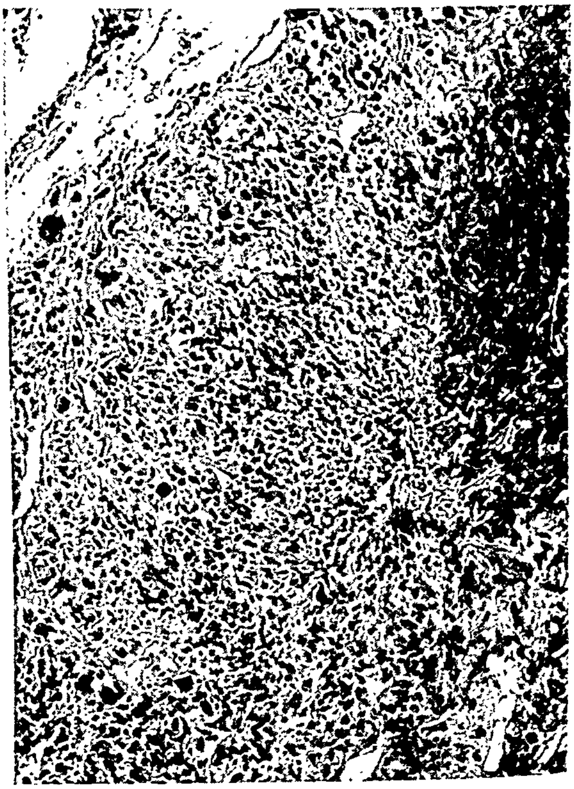

Fig. 5.—Section from retro-orbital tumor.

siderable new bone formation was seen at the fracture site in the last progress roentgenogram of the left femur (fig. 6*B*), made on Sept. 10, 1958.

In late September, 1958, she began having episodes of dizziness with loss of memory lasting an hour or more, probably the result of cerebral metastases. Word was received that the patient died quietly at home on Oct. 24, 1958. No autopsy was performed.

Comment

In this case as in others in the literature the question arises whether the patient had multicentric tumors or a primary tumor with delayed appearance of metastases. If this was an example of the latter, the host was able through unknown biological factors to suppress growth of the neoplasm for 18 years. If this was an instance of the multicentric origin of malignancy, it would be most unusual for this patient to have had two rare, yet identical, primary tumors.

Kelly and Cullen,[3] in a discussion of the clinical history of cases of myosarcomas of the uterus, indicated that patients usually came with a definite history of uterine myomas of several years' duration. Myomas which have increased slowly for years may suddenly grow rapidly without becoming malignant. Ogasawara and Tamura[4] reported an instance of a fibromyosarcoma which became malignant after 35 years.

In our opinion this case represents delayed appearance of metastases. Biological factors which determine the balance in the host-neoplasm relationship are not understood. Our patient did not receive estrogen therapy in relation to the appearance of the secondary malignancy. This was a slowly growing tumor which permitted the patient to survive for three years after the onset of symptoms of the terminal illness. Sylven[5] reported a case in which metastases occurred in the axilla and extended into the thoracic cavity causing involvement of the fourth rib 19 years after hysterectomy for leiomyosarcoma.

Wheelock and Warren[6] stated that a correct diagnosis of leiomyosarcoma of the uterus could be made on morphologic findings and that the diagnosis did not require confirmation of invasion, metastases, and/or recurrence. Finn[7] reported an erroneously diagnosed leiomyosarcoma, which was considered a benign cellular myoma until metastases developed. Chang and co-workers[8] called attention to the divergence of opinion regarding the reliability of histological criteria for the diagnosis. If metastases are a criterion of malignancy in borderline cases patients must be followed for many years to confirm the diagnosis.

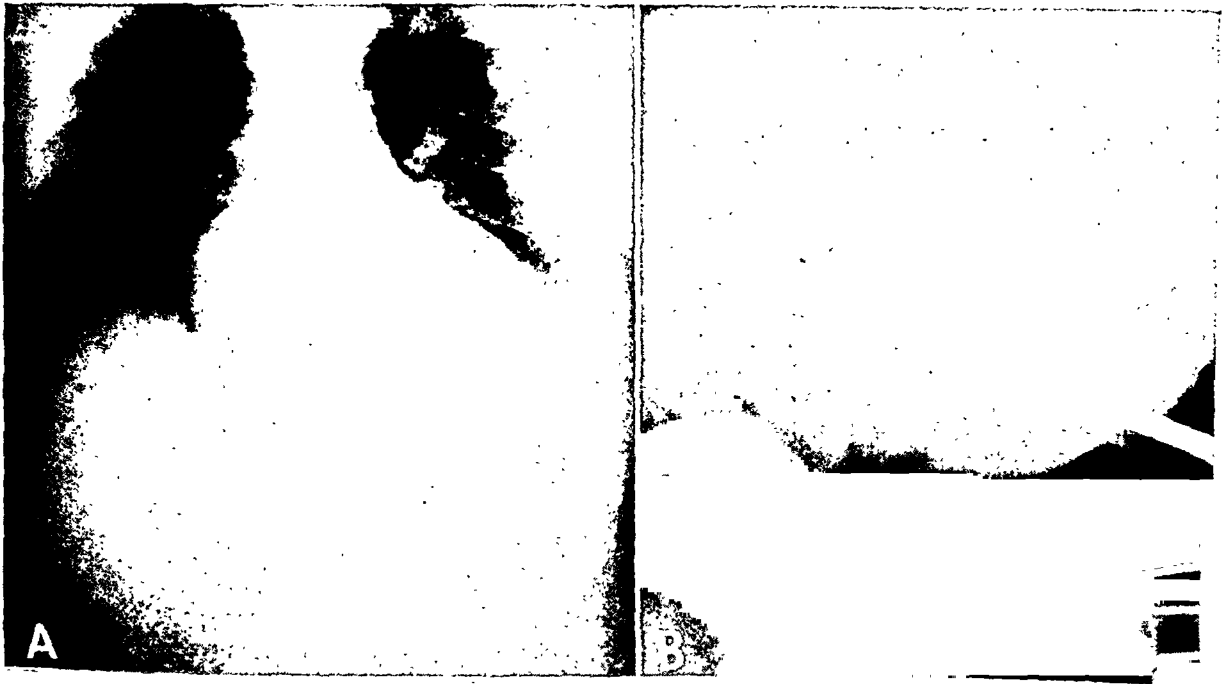

Fig. 6.—*A*, roentgenogram of chest, showing 2 cm. circular density in left lung field, probably due to metastatic leimyosarcoma. *B*, roentgenogram of left femur, taken Sept. 10, 1958. New bone formation is present.

Bone metastases are exceedingly rare, except for those involving ribs and vertebrae. The table shows a compilation of the data on bone metastases found in the literature not including a few undocumented reports of rib and vertebral involvement.

As noted in the table there have been four cases reported with metastases to the long bones. Our case brings the total to five.

We have been able to find one other case, that reported by Gardner,[9] in which there were metastases to the retro-orbital region. Our case, therefore, is the second of these reported in the literature.

Reported Bone Metastases from Leiomyosarcoma of the Uterus

Source	Cases, No.	Age, Yr.	Longevity	Metastases, Location
Blackman, S.: Personal communication to Brooke, W. S., and Thomason, J. R.	1	Unknown	Unknown	Skull
Brooke, W. S., and Thomason, J. R.: Arch. Surg. **51**:120-124 (Sept.) 1945.	1	48	5 yr.	Osteolytic lesion of left femur with fracture
Decio, C.: Riv. ital. di ginec. **22**:640-646 (Sept.) 1939.	1	55	1 yr. 10 mo.*	Humerus
Gardner, L. F.[9]	1	55	4 yr.	T-1, 3 ribs, and right retro-orbital region
Grynfeltt, E.: Bull. de l'Assoc. franç. p. l'etude du cancer, **16**:447-467 (June) 1927.	1	70	2 yr. 4 mo.*	Femur
Miller, R. H., and Rogers, H.: New England J. Med. **198**:927-931 (June 21) 1928.	1	40	Less than 1 yr.	Right hip with fracture
Robbins, L. L.: Arch. Surg. **47**:463-467 (Nov.) 1943.	2	46	10 yr.	Osteoblastic lesions of lumbar vertebrae
		50	1 yr.*	Osteoblastic lesions of lumbar vertebrae
Sylven, B.[5]	3	65	19 yr.*	Axilla involving rib
		58	"rapidly succumbed"	Right maxilla and T-9
		49	"some months"	Right acromion and scapular spine with fracture

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* Still alive when reported.

Summary

In an unusual case of leiomyosarcoma of the uterus metastases became symptomatic 18 years after total hysterectomy. This case is the fifth reported in the literature with metastases in the long bones and the second with retro-orbital metastases. The possibility evidently exists for the recurrence of leiomyosarcoma many years ofter excision of the primary lesion.

Box 849, Williamson, W. Va. (Dr. Drake).

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DIAGNOSIS BY A DATA-PROCESSING MACHINE.—The claim is frequently advanced that the process of drawing correct diagnostic inferences from a patient's symptoms is in large part indefinable and intuitive. It is the purpose of this communication to show that the making of correct diagnostic interpretations of symptoms can be a process in all aspects logical and so completely defined that it can be carried out by a machine. The machine chosen for this demonstration is a conventional high-speed electronic data-processing system, programed to make diagnostic decisions in a manner analogous to that of an unbiased physician. . . . The diagnostic significance of symptoms was determined and a statistical diagnostic method developed with data referring to 5,929 consecutive adult white patients . . . admitted to the outpatient departments of the New York Hospital during the 18-month period beginning July 1, 1948. The method was tested with data referring to 2,745 consecutive adult white patients (1,280 men and 1,465 women) admitted during the 12-month period beginning Jan. 1, 1956. Each patient's symptoms were elicited through a printed form, the Cornell Medical Index-Health Questionnaire (abbreviated CMI). . . . From data on the CMI alone, and at the rate of 1 second per patient, the machine correctly identified in 2,745 patients the presence of these 60 diseases 44% of the times they had been found on hospital examination. A physician and the machine independently interpreted the CMIs of 350 patients who underwent comprehensive medical investigation. The physician correctly identified 43% of diseases studied, other than psychoneurosis, when they had been diagnosed in the hospital, while the machine correctly identified 48%. The physician correctly identified 81% of instances of psychoneurosis, while the machine identified 42%. Of all the diagnoses made by the physician, 2% were false, as were less than 5% of those made by the machine.—K. Brodman, M.D., and others, Interpretation of Symptoms with a Data-Processing Machine, *A. M. A. Archives of Internal Medicine,* May, 1959.

ERYSIPELAS IN PREGNANCY

REPORT OF A CASE WITH FATAL OUTCOME

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and
Rosemary Clark, M.D., San Francisco

Information on the association of erysipelas with pregnancy is rare. A 32-year-old woman, para 3, gravida 7, six weeks before her expected date of delivery noted a slight swelling over the right cheek. It persisted, and she was treated with ACTH and diphenhydramine hydrochloride. Several days later she was hospitalized with edema, erythema, induration of the face and neck, and a temperature of 38.6 C (101.5 F). Chlortetracycline and meperidine hydrochloride were included in therapy. Cultures disclosed hemolytic streptococci. The disease process extended to the upper one-fourth of the chest, and therapy with erythromycin was started. A living girl in good condition was delivered. Several hours later blood pressure had dropped to 84/70 mm. Hg. Whole blood, hydrocortisone, lanatoside C, streptomycin, and levarterenol bitartrate were given, but the patient became cyanotic and died. The anatomic diagnosis was erysipelas with acute cellulitis of the face, neck, and chest; acute mediastinitis involving the pericardium and pleurae with pleural effusion; and acute congestion of the viscera. Pregnancy undoubtedly was a factor in the outcome.

Report of this case was prompted by both the relative scarcity of erysipelas in the present era and the infrequency with which this disease leads to maternal death. With the advent of the sulfonamide and antibiotic drugs, reports concerning this disease have become increasingly uncommon. Reports published in the past four decades implicating erysipelas as a cause of morbidity or mortality in pregnancy are extremely rare. One must rely on isolated articles and fleeting references in the older obstetric textbooks concerning this condition in association with pregnancy.

Siegmund[1] reported a case of erysipelas with early phlegmon formation involving the external genitalia, perineum, hip region, and lower part of the abdomen in a 28-year-old primipara, resulting in her death 22 hours post partum. Death apparently was the result of overwhelming infection and toxicity due to streptococcic cellulitis of the aforementioned areas. No evidence of peritonitis or involvement of the internal genitalia was present at autopsy. The similarity in the agonal stage of this patient's case to the one reported here is striking. Her reaction to the infection was also similar. In the case described by Siegmund the baby did not survive, dying one day after birth. Postmortem examination of the baby showed an intracranial hemorrhage.

Lubin[2] reported the case of a 25-year-old patient who developed erysipelas of the face and leg, at term, after a sore throat. The outcome was good for the mother and baby in spite of multiple areas of infection, prolonged convalescence, and the fact that chemotherapy and antibiotic drugs were not available at the time.

Keefer and Spink[3] reported a general mortality from erysipelas of 16.4 ± 3.6% prior to the use of chemotherapy. With the advent of the sulfonamide drugs mortality fell to 2.4% according to Hoyne, Wolf, and Prim.[4] With the employment of antibiotics, particularly penicillin, the prognosis for this disease has been significantly improved. According to Snodgrass and co-workers,[5] who observed a mortality of 2.06% in patients with erysipelas treated with sulfonamide preparations, several factors are known to influence the course of the disease. They are (1) duration of the disease before treatment, (2) age of the patient, (3) severity of the infection, and (4) associated diseases.

According to Williams[6] any septic condition has a more serious prognosis in pregnancy than at other times. Adair and Stieglitz, in their textbook "Obstetric Medicine,"[7] stated that erysipelas is not often observed in pregnancy but that the prognosis is not necessarily unfavorable, especially if the disease is limited to the face or neck. However, if the infection extends to the back or chest the situation becomes more serious whether the woman is pregnant or not. They further stated that the prognosis of erysipelas involving the pubic or inguinal regions is more serious because of the possible spread and resulting peritonitis.

Williams has stated that, in cases of erysipelas which occur during pregnancy, the chief concern is the possible development of puerperal infec-

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tion or septicemia rather than the local spread and the possible cross-infection to other patients. Transmission of the disease to the child has been rarely observed. DeLee[8] noted that when this disease attacks parts of the body other than the genitalia the danger is less, but records show that puerperal infection may result. The author stated that he delivered a patient suffering from facial erysipelas. Shortly after birth the vulva became involved, after which the patient died of acute sepsis. The autopsy showed streptococcic peritonitis.

Report of a Case

A 32-year-old woman, para 3, gravida 7, had had the usual childhood diseases including uncomplicated scarlet fever. Her obstetric history included an infected incomplete abortion in 1950 at four and one-half months and an uncomplicated incomplete abortion in 1955 at two and one-half months. Three living children were normally delivered in 1951, 1952, and 1956. The pregnancies and puerperiums were uneventful. The patient gave a history of cutaneous reaction to penicillin and allegedly was sensitive to many other drugs. Her mother had died aged 55 from hypertension and hypertensive heart disease. Her father had died aged 63 from similar causes.

The patient's last menstrual period occurred Nov. 6, 1956, making her expected date of delivery Aug. 13, 1957. Her antepartum course was uneventful until July 1, 1957, when she noted a slight swelling over the right cheek which developed after an insect bite, presumably from a spider. She was seen the next day by her family physician, who administered a calcium preparation and prescribed an antihistamine. The swelling persisted and was associated with a moderate amount of discomfort. She was seen the following day by another physician, who gave her a second injection and prescribed cold compresses. No improvement was noted, and the patient consulted a dermatologist on July 5, 1957, at which time there was swelling of the right cheek and the bridge of the nose. There was associated pain and tenderness extending to the angle of the jaw on the right side. No cervical adenopathy was noted, and the parotid regions and oral cavity were normal. The patient's pulse and temperature were normal. An intramuscular injection of 30 mg. of ACTH was given, diphenhydramine hydrochloride, 50 mg. three times daily by mouth, was prescribed, and the patient was instructed to apply ice packs to her face. She was again seen on July 8, 1957, at which time the edema had extended to the forehead and right ear, but the swelling of the right cheek had diminished. Administration of 30 mg. of ACTH was repeated and previously prescribed medication continued in addition to 5 mg. of prednisone, three times daily. The temperature, taken three times daily by the patient, remained normal.

On the early morning of July 10, 1957, the patient was seen at her home by the dermatologist because of increased pain and a temperature of 38.8C (101.8F). The edema had spread over her entire face, chin, and neck. Since she had given a previous history of penicillin sensitivity, therapy was started with chlortetracycline, 500 mg. by mouth every six hours.

The patient was admitted to the Mount Zion Hospital on July 10, 1957. At this time there was a warm, tender, red swelling of the face and neck, extending to just above the clavicles. No definite border was discernible. At physical examination the patient's temperature was 38.6C (101.5F); pulse, 90 per minute; respirations, 36 per minute; and blood pressure, 140/60 mm. Hg. The patient was a well-developed, well-nourished woman, acutely ill, with edema, erythema, and induration of the face and neck. The cervical lymph nodes were not palpable. Erythema of the tympani with a hemorrhagic crust in the left auditory meatus was noted. Her tongue was dry, coated, and furrowed. No involvement of the salivary glands or oral cavity was present. Her lungs were clear to auscultation and the heart was of normal size with sounds of good quality and no murmurs. Rhythm was normal, and the pulse rate continued at 90. Her abdomen was protuberant; she was in the 36th week of pregnancy, and fetal movements were present. The fetal heart tones were normal. She had external hemorrhoids.

Pertinent laboratory findings included: hemoglobin concentration, 10.9 Gm.% or 70% of normal; packed blood cell volume, 35; white blood cell count 12,300 per cubic millimeter (filamented cells, 62%; nonfilamented cells, 32%; lymphocytes, 1%; monocytes, 4%; and metamyelocytes, 1%). Sedimentation rate was 57 mm. per hour; when corrected according to the method of Hynes and Whitby[8A] it was still markedly elevated.

Her urine was amber with pH, 6; sugar, 3+; with a trace of acetone and no diacetic acid; protein, 2+; white blood cells, two per high-power field; red blood cells, occasional per high-power field; bacteria, moderate; specific gravity, 1.025. Blood sugar determination was 138 mg. %. Result of serologic test for syphilis was negative.

Progress and Treatment.—Therapy was continued with chlortetracycline, 500 mg. every six hours; meperidine hydrochloride, 50 mg. every four hours for pain; diphenhydramine hydrochloride, 50 mg. every four hours; and cold compresses were applied to the patient's face and neck. Smears taken from the left ear and from the bullae which soon developed on the neck showed gram-positive cocci, and cultures disclosed hemolytic streptococci which were sensitive to tetracycline, penicillin, and streptomycin.

By 4 p. m. on the day of admission the patient's temperature became further elevated to 39.3C (102.7F), and by 8 p. m. the disease process had extended to the upper one-fourth of the chest, with hemorrhagic bullae appearing on the skin in this region. A definite advancing border was observable. The temperature soon dropped to 37.7C (100F), pulse, 98, and the patient seemed more comfortable. Erythromycin, 500 mg. by mouth every six hours, was given in addition to the chlortetracycline.

At 1:45 a. m., July 11, 1957, the patient precipitously delivered, in bed, a living girl, weighing 6 lb. 4 oz. (2,381 Gm.), whose condition was good. Examination immediately post partum revealed no lacerations or abnormal bleeding. The blood pressure was 128/80 mm. Hg; pulse, 100; and respirations, 24 per minute. The patient's condition remained unchanged until 6:15 a. m. when the blood pressure dropped to 98/78 mm. Hg, the pulse rose to 126, and respirations were 26 per minute. The onset of moderate dyspnea was noted. A solution of 5% dextrose in distilled water was administered intravenously, and 2 cc. of methoxamine hydrochloride was given. Oxygen was also administered, by nasal catheter. By 8 a. m. the blood pressure was 84/70 mm. Hg, pulse, 90, respirations, 24 per minute, and temperature, 37.8C (100F). Laboratory studies on the blood done at this time revealed a hemoglobin concentration of 17.8 Gm.% or 115% of normal, with a white blood cell count of 6,100 per cubic millimeter, with a differential count of filamented cells, 34%; nonfilamented cells, 39%; lymphocytes, 17%; and metamyelocytes, 9%. The packed blood cell volume was 56.

The patient was given 500 cc. of whole blood. A second 500 cc. of 5% dextrose in distilled water, to which was added 100 mg. of hydrocortisone, was administered intravenously. Lanatoside C (8 mg.) was given slowly intravenously because of progressive shock, increasing gallop rhythm, and sinus tachycardia. Streptomycin, 0.5 Gm. every 12 hours, was ordered. For a brief period the patient showed improvement. However, at 12 noon her blood pressure dropped to 60/0 mm. Hg, the pulse rate rose to 140, and respiratory distress increased. Levarterenol bitartrate was added to the fluids being given intravenously, as well as an additional 4 mg. of lanatoside C and 100 mg. of hydrocortisone. The patient failed to rally. She became cyanotic and died at 12:45 p. m. The baby, whose condition remained good, was discharged four days later.

Postmortem Findings.—Gross findings at postmortem examination in the mother included cyanosis of the lips, oral mucosa, and ears. The skin of the cheeks, lower part of the face, neck, and upper anterior thorax was edematous and purplish-red. Small blebs were present in the region of the lower part of the neck and upper part of the chest. The lower parts of the legs showed minimal pitting edema. Autopsy revealed that the pleural cavities contained clear fluid (800 cc., left, and 500 cc., right) in which floated yellow fibrinous clots. The organs, including the brain, were acutely congested. No other gross pathological changes were present except as follows: The lungs had undergone partial collapse of the lower lobes. The liver was enlarged and weighed 3,000 Gm., and an abnormal amount of blood oozed from its cut surface. The uterus was enlarged, consistent with the postpartum status.

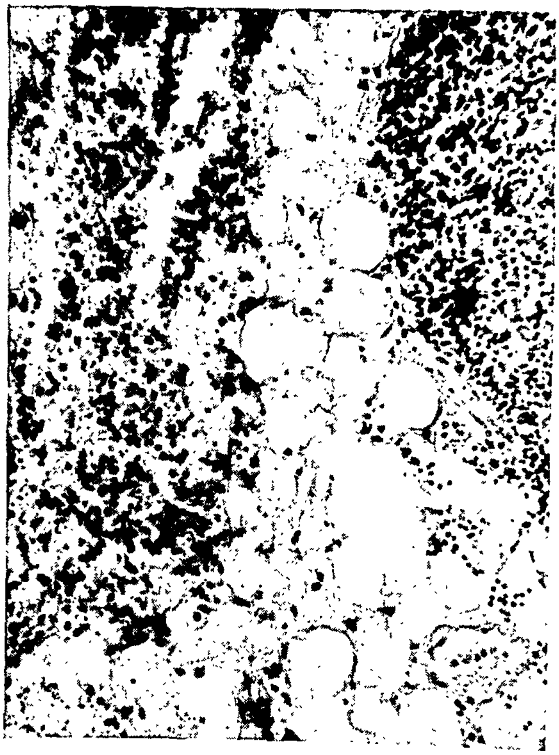

Fig. 1.—Mediastinal tissue, showing cellular infiltrate *(left)* and thymic tissue *(right)*.

Microscopic Findings.—The significant microscopic findings were an acute inflammatory reaction involving the subcutaneous tissues of the neck and chest and involvement of the mediastinal areolar and lymphoid tissues (fig. 1), the external surfaces of the pericardium (fig. 2), the thymus gland, and portions of the pleurae. These tissues contained scattered foci of necrosis and a mixed cellular infiltrate of polymorphonuclear leukocytes, small mononuclear cells, and monocytes. Associated with the necrotic material were bacterial colonies composed of gram-positive cocci. The other organs were altered by severe acute congestion but were otherwise normal. Material from the uterus and blood from the heart were taken at autopsy and cultured for anaerobic and aerobic organisms. The cultures failed to show any bacterial growth.

The anatomic diagnosis was erysipelas (Streptococcus pyogenes) with acute cellulitis of the face, neck, and chest; acute mediastinitis involving the pericardium and pleurae with pleural effusion; and acute congestion of the viscera. The only other finding was of the postpartum state of the uterus.

Comment

Mortensen,[9] in a study of 150 cases of erysipelas comparing the results of therapy with sulfonamide drugs to those with penicillin, showed that the latter is the preferred drug since it gave the quickest cure, as assessed by the course of the temperature and the subsidence of the cutaneous manifestations. Schembra [10] recommended combined treatment with sulfonamides and penicillin in severe cases of erysipelas; Griffith [11] reported three severe cases of erysipelas treated successfully with erythromycin; and Welsh [12] recommended the use of parenterally administered penicillin, 600,000 units daily, or orally administered chlortetracycline, oxytetracycline, or tetracycline hydrochloride, 500 mg. every six hours. Each of these drugs was effective in the treatment of erysipelas.

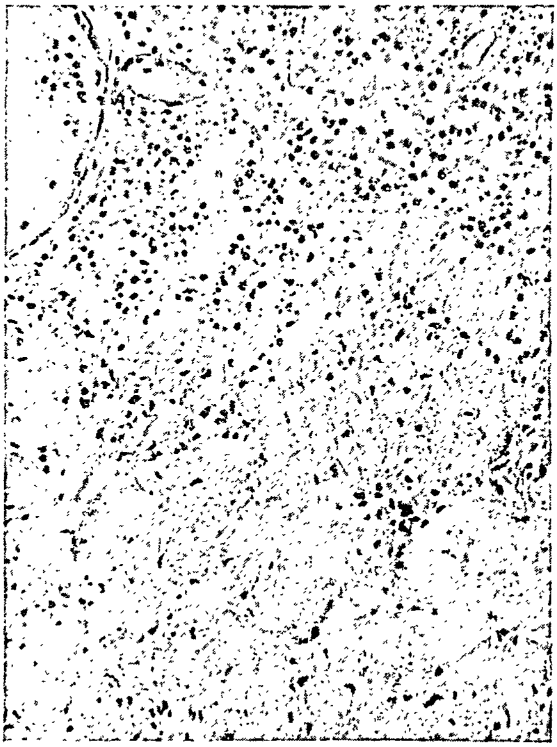

Fig. 2.—Pericardium, showing cellular infiltrate of polymorphonuclear leukocytes, small mononuclear cells, and monocytes (*upper left*).

The unfortunate outcome of the case reported here leads to the conclusion that we were dealing with a rapidly developing and fulminating infection following on the footsteps of a prolonged allergic reaction to an insect bite. This developed in a patient whose pregnancy undoubtedly was a critical factor in the outcome. A possible reason for this is the increased amount of corticosteroids present during pregnancy, perhaps masking or altering the early manifestations of the infection and presumably permitting the spread of the process in spite of antibiotic therapy. Whether parenterally administered antibiotics instituted earlier in large doses would have altered the picture is a matter for conjecture, especially in the light of Lubin's case, in which the patient survived without the advantage of chemotherapy or antibiotics. The dramatic rapidity of the development of the serious manifestations allowed no time for effective alteration of therapy.

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NEW ANTICOAGULANT FOR ORAL USE—3-(1'-PHENYLPROPYL)-4 HYDROXYCOUMARIN (LIQUAMAR)

ITS EVALUATION FOR SHORT-TERM THERAPY

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One hundred eleven patients received short-term anticoagulant therapy with 3-(1'-phenylpropyl)-4 hydroxycoumarin. After a loading dose of 30 mg., a prophylactic (prothrombin time of 20 to 25 seconds) or therapeutic (prothrombin time of 25 to 30 seconds) response was obtained within an average of 42 hours in 77% of the patients. After this induction period, a 6.4-mg. (average) maintenance dose resulted in protective prolongation of the prothrombin time (20 to 35 seconds) in 88% of the patients within 66 hours after administration of the loading dose. Some patients received heparin and the new anticoagulant combined.

A new coumarin derivative is 3-(1'-phenylpropyl)-4 hydroxycoumarin (Liquamar), with a therapeutic action 10 to 25 times that of bishydroxycoumarin, the parent substance. This drug has been the subject of intense laboratory and clinical evaluation in Europe,[1] but only a few studies have been reported in the United States.[2] Even in very small doses, it decreases blood coagulability by inhibiting the formation of prothrombin and factor VII (autoprothrombin I) but has no effect on the Christmas factor (autoprothrombin II), the concentration of which is lowered by other orally given anticoagulants such as bishydroxycoumarin, acenocoumarol, phenindione, and diphenadione. In some patients this may be significant in view of the fact that the widely used Quick one-stage prothrombin time test does not reflect changes in the level of the Christmas factor.

We wish to report on the use of Liquamar in 111 patients for short-term oral anticoagulant therapy. They were all hospitalized because of acute vascular disease. Eighty had acute myocardial infarction, 9 coronary insufficiency, 12 acute phlebitis, 5 acute pulmonary infarction, 3 atrial fibrillation with cerebral embolism, 1 atrial fibrillation with iliac artery embolus, and 1 acute retinal vein thrombosis. Seventy-one patients were male and 40 were female; 3 were Negro and the rest were Caucasian. Their ages ranged from 34 to 84 years; 90% of them were in the fifth to the ninth decades of life. The prothrombin time test was performed according to the Quick one-stage technique, and the results were reported in seconds, the normal control time being from 12 to 14 seconds. An initial prothrombin time was obtained for each patient, after which a loading dose of Liquamar was given. Thereafter, a daily prothrombin time test was performed, and the maintenance dose of anticoagulant was adjusted individually in an attempt to secure prothrombin time values within the therapeutic range of 25 to 35 seconds. This offers maximum protection with a minimum of risk of bleeding complications inherent in a state of drug-induced hypocoagulability. A prophylactic prothrombin time level of 20 to 25 seconds offers moderate protection and is the routine goal of long-term anticoagulant therapy. This study covered a period of anticoagulant therapy of 2 to 39 days, with an average of 18.8 days.

Results of Therapy

Group 1 consisted of 46 patients who received a loading dose of 30 mg. of Liquamar. Its anticoagulant effects were as follows: After an average interval of 16 hours, the prothrombin time of 6 patients (16.6%) had reached prophylactic levels of 20 to 25 seconds, but in 32 (83.4%) it remained below 20 seconds. After an average interval of 40 hours, the prothrombin time was still less than 20 seconds in 10 patients (22.7%); it had reached the prophylactic range of 20 to 25 seconds in 14 (31.8%) and the therapeutic levels of 25 to 35 seconds in 20 patients (45.4%). After an average interval of 66 hours, the prothrombin time was unchanged (20 to 25 seconds) in two patients, was decreased in nine (three showed less than 20 seconds, three had prophylactic values of 20 to 25 seconds, and three showed therapeutic values of 25 to 35 seconds), and was increased in seven (five were within the therapeutic range and two showed "overshooting"—more than 40 seconds). After an average interval of 90 hours, the prothrombin time showed a drop in four patients (two were in the prophylactic range of 20 to 25 seconds and two were within the therapeutic range of 25 to 35 seconds) and a further rise to 41 seconds in one patient. This subject still had a prothrombin time of 29 seconds (control 12 seconds) when retested on the ninth day after ingestion of the 30-mg. loading dose.

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Twenty-six patients of group 1 received the first maintenance dose of Liquamar after an induction period of about 42 hours after the loading dose. It varied from 1.5 to 9 mg. (average 6.4 mg.), depending on the recorded individual prothrombin time. When retested on the next morning, 3 patients still had prothrombin values below 20 seconds, 11 were in the prophylactic range of 20 to 25 seconds, and 12 were in the therapeutic range of 25 to 35 seconds. Subsequently, the entire group of 46 patients received maintenance doses of the drug adjusted on the basis of the daily prothrombin time. The average individual maintenance dose varied from 1.5 to 7.5 mg., with a group average maintenance dose of 4.0 mg.

Group 2 consisted of 36 patients who received a loading dose of 21 mg. of Liquamar. Its anticoagulant effects were as follows: After an average interval of 18 hours the prothrombin time reached prophylactic levels of 20 to 25 seconds in 8 patients (22%), 7 of whom had a high initial prothrombin time, while it remained below 20 seconds in 27 patients (78%). After an average interval of 40 hours the prothrombin time was less than 20 seconds in six patients while it showed an increase, from the prophylactic to the therapeutic range, in three patients. Two of the latter were retested 24 hours later. One showed a drop in the prothrombin time to 20 seconds (control 13 seconds) while the other remained unchanged at 34 seconds (control 14 seconds).

Twenty-six patients received the first maintenance dose of 9 mg. about 24 hours after ingestion of the 21-mg. loading dose; thus they received in a fractional manner an amount of Liquamar equivalent to the loading dose of group 1. When they were tested the next morning, about 41 hours after administration of the loading dose, the prothrombin time was still less than 20 seconds in 7 patients (26.9%); it had reached the prophylactic range of 20 to 25 seconds in 11 (42.3%) and the therapeutic levels of 25 to 35 seconds in 8 (30.7%). Their initial prothrombin time was of the same order of magnitude as in group 1 with the exception of three patients whose values were somewhat prolonged (17 seconds, control 12 seconds). However, in contrast to the findings in group 1, only one patient had a prothrombin time of 37 seconds (control 14 seconds); most of them were closer to the minimum than to the maximum values of the prophylactic or therapeutic range.

Each patient of group 2 received subsequent doses of Liquamar ranging from 1.5 to 12 mg., depending on the individual daily prothrombin time. The average individual maintenance dose varied from 2.2 to 7.6 mg., and the average group maintenance dose was 4.0 mg.

Group 3 consisted of six patients. Three were given a loading dose of 27 mg. and three 24 mg. of Liquamar. Their response was not significantly different from that of groups 1 and 2.

Group 4 consisted of 21 patients. They received both heparin sodium and Liquamar. The former was given either intravenously or subcutaneously or both, whenever the need for prompt anticoagulant effect was deemed necessary, such as in the presence of pulmonary infarction, phlebitis, and myocardial infarction with delayed diagnosis. Heparin administration was discontinued when the prothrombin time had reached at least the prophylactic level of 20 seconds or more. Eight patients received a loading dose of 30 mg. of Liquamar, while the administration of heparin was continued for a period of 19 to 44 hours. The response was similar to that in group 1. The average individual maintenance dose varied from 2.1 to 6 mg., with a group average of 4.3 mg.

Three patients were given a loading dose of 24 mg., and eight patients received 21 mg. of Liquamar in addition to the heparin. The latter therapy was continued for a period of 12 to 92 hours, with an average of 45 hours. The pattern of response in this group of patients was similar to that in group 2. The individual average maintenance dose varied from 2.0 to 7.7 mg., with a group average of 5.1 mg.

One patient received a loading dose of only 15 mg. (high initial prothrombin time) in addition to the heparin therapy, which was discontinued at the end of 12 hours. The response to the orally given anticoagulant was satisfactory. Another patient was given two daily doses of 12 mg. of Liquamar in addition to heparin. At the end of 38 hours a prophylactic level had been reached.

On cessation of anticoagulant therapy, prothrombin time determinations were done for a variable number of days in 58 patients treated with Liquamar alone. A significant prolongation to 20 seconds or more was recorded for more than one day in 23 patients, two days in 1, more than two days in 11, three days in 1, more than three days in 6, four days in 5, more than four days in 7, for five days in 1, more than five days in 2, and more than seven days in 1. These findings indicate that Liquamar has a moderately prolonged effect on blood coagulability.

Undesirable Effects

In the course of anticoagulant therapy some undesirable effects may be encountered.

Poor Response.—Poor response was considered to be present during oral anticoagulant therapy whenever the patient's daily prothrombin time fell below 20 seconds. Usually it was the result of our underestimation of the amount of the drug required for maintenance of the prothrombin time within the therapeutic range. Occasionally, a refractory patient was encountered. During their entire treatment period, nine patients of group 1 displayed one or two days of poor response. In group 2, six patients had one day of poor response, one had two such days, two had three such days, and one had four such days. In group 4, five patients had one or two days of poor response. This lower incidence is attributable to the smaller number of patients involved and the shorter duration of treatment, average 9.8 days as compared to the average 21 days for groups 1 and 2.

"Overshooting."—"Overshooting" was recorded in 24 of 90 patients treated with Liquamar alone, an incidence of 26.6%. Ten patients had prothrombin times in excess of 40 seconds during the first five days of treatment, presumably the result of the loading dose. Seven patients (15.2%) had received the 30-mg. dose and three (8.3%) the 21-mg. dose. This overshooting lasted one day in six patients, two days in two, and three days in two. Ten patients (21.7%) of group 1, seven (19.4%) of group 2, and one (12.5%) of group 3 displayed overshooting during the midperiod of anticoagulant therapy. This overshooting lasted one day in 11 patients, two days in 3, three days in 1, four days in 1, six days in 1, and eight days in 1 patient. In two subjects overshooting that lasted one day occurred toward the end of the course of therapy. A few of the patients displayed overshooting in both the early and middle periods of treatment, which accounts for the discrepancy in the totals. An occasional patient displayed both poor response and overshooting during a single course of treatment. In most instances overshooting was the result of too large a maintenance dose, although a few very sensitive patients reacted excessively to an otherwise small dose of Liquamar.

When overshooting was excessive, even though unaccompanied by bleeding phenomena, it was easily corrected by the use of fractional doses (2.5 to 10 mg.) of vitamin K_1 given orally at suitable intervals. Thus, we were able to avoid the development of refractoriness to Liquamar.

Bleeding Complications.—Four episodes of frank bleeding occurred in our series, an incidence of 3.6%. The bleeding showed as gross hematuria, but one of the patients also displayed a subconjunctival hemorrhage. All patients recovered without complications or sequelae. In two instances, the hematuria occurred four days after the peak of the overshooting, when the prothrombin time had spontaneously dropped to within the therapeutic range. In the third instance the prothrombin time had ranged between 35 and 36 seconds for seven days before the patient developed hematuria. The fourth patient, with overshooting (42 seconds) for one day, had remained asymptomatic, but six days later, after the prothrombin time had been well within the therapeutic range for three days (28.5 seconds), bleeding appeared. This lack of direct correlation between prothrombin time and the evidence of bleeding phenomena was striking in our cases.

Vitamin K_1 was used both intravenously and by mouth when bleeding complications appeared. The dose varied between 5 and 50 mg.; its effect was prompt and satisfactory. Similarly, this drug was used to normalize the prothrombin time in two of our patients in preparation for emergency surgery.

Comment

A suitable loading dose is one that produces a satisfactory prolongation of the prothrombin time within the shortest period of time with a minimum risk of overshooting and bleeding. Our experience leads us to suggest that the 30-mg. dose meets these requirements. The smaller dose should be reserved for patients with a higher than normal initial prothrombin time. In this respect our findings agree with those of Brambel,[11] who favored a 30-mg. loading dose. On the other hand, Toohey [18] found this dose to be excessive because of a high incidence of overshooting and suggested the use of 24 mg. as the loading dose. Priest and Pauli [20] used various loading doses from 30 to 51 mg. and found no significant difference in response. In their series prophylactic levels were attained within 40 hours on the average, and therapeutic levels were demonstrated after 64 hours. The larger the loading dose, the shorter the induction period and the greater the incidence of overshooting, which these authors believe to be an acceptable risk.

Of our patients, 77.3% showed a prophylactic or therapeutic response within an average of 42 hours after the 30-mg. loading dose of Liquamar had been given. Thereupon the ingestion of an additional average maintenance dose of 6.4 mg. increased the incidence of protection to 88% of the patients when tested 66 hours after administration of the loading dose.

The maintenance dose varied from 1.5 to 12 mg. with an average of 4.0 mg. This is in agreement with the published results. Liquamar produces a moderately prolonged state of hypocoagulability of the blood as judged by the Quick one-stage prothrombin time. Individual as well as day to day variation was, however, noted in many of our subjects. Daily prothrombin time determinations are advisable in order to secure the best results. The incidence of poor response (prothrombin time of less than 20 seconds) was low. Only occasionally does one encounter a resistant patient. This confirms similar findings of Brambel and others.[3] Overshooting at some time during the course of treatment occurred in 26.6% of our patients. Excessive prolongation of the prothrombin time within five days of the 30-mg. loading dose occurred in 15.2%. This is in contrast to an incidence of total and early overshooting of

13.7 and 8.3%, respectively, reported by Priest and Pauli.[2d] Differences in experimental approach probably account for this. Our experience with early overshooting is similar to that of Priest and Pauli; no bleeding resulted therefrom. On the other hand, late overshooting may lead to significant hemorrhagic manifestations. The availability of vitamin K_1 for oral use allows for greater flexibility and ease of management of overshooting, as has been pointed out by Ensor and Peters.[2c]

The incidence of bleeding was low, 3.6%, which is similar to that reported by Priest and Pauli. These authors have reported an over-all incidence of bleeding of 4.5% in 641 patients on short-term therapy with Liquamar recorded in the literature. If to these figures are added the 1,080 coronary, phlebitis, and postpartum patients treated by Ensor and Peters without any bleeding complications, one must conclude that Liquamar is a safe anticoagulant and that its use is accompanied by a low risk of hemorrhage. Our experience with vitamin K_1 is similar to that of other investigators. It effectively normalizes the hypoprothrombinemia induced by Liquamar. The dosage and route of administration should be individualized so as to correct either dangerous overshooting or bleeding without producing a refractory state in case further therapy with Liquamar is considered advisable.

The results obtained in patients of group 4 demonstrate the feasibility of combining heparin for its prompt anticoagulant effect and Liquamar, which induces hypoprothrombinemia after a short induction period. Although not the ideal anticoagulant, Liquamar produces a more satisfactory, smoother, and less complicated state of blood hypocoagulability than that obtained with other anticoagulants such as bishydroxycoumarin (Dicumarol), ethyl biscoumacetate (Tromexan ethyl acetate), and phenindione (Hedulin) used by us in the past.

Summary

One hundred eleven patients received short-term anticoagulant therapy with 3-(1′-phenylpropyl)-4 hydroxycoumarin (Liquamar). Some received heparin and Liquamar combined. After a loading dose of 30 mg. had been given, a prophylactic (prothrombin time of 20 to 25 seconds) or therapeutic (prothrombin time of 25 to 35 seconds) response was obtained within an average of 42 hours in 77% of the patients. After this induction period, the ingestion of a 6.4-mg. (average) maintenance dose resulted in the development of protective prolongation of the prothrombin time (20 to 35 seconds) in 88% of the patients within 66 hours after administration of the loading dose. The maintenance dose varied between 1.5 and 12 mg., with an average of 4.0 mg. Daily determination of the prothrombin time provides an excellent guide to therapy.

A smaller, 21-mg. loading dose should be given if the initial prothrombin time is somewhat prolonged above the normal. Because of the induction period of about 48 hours that usually follows a loading dose of Liquamar, heparin may also be given if immediate anticoagulant action is desired.

Hematuria and one subconjunctival hemorrhage were the bleeding complications that occurred in 3.6% of the cases. Complete recovery ensued. Vitamin K_1 should be given orally or parenterally in small repeated doses (2.5 mg. to 50 mg.) to correct "overshooting" (prothrombin time greater than 40 seconds) or bleeding. Liquamar produces a satisfactory state of blood hypocoagulability during short-term therapy of thrombovascular disease states.

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The coumarin derivative used in this study was supplied as Liquamar by Organon, Inc., Orange, N. J.

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CLINICAL NOTES

SUCCESSFUL TREATMENT BY A CHEST BLOW OF CARDIAC ARREST DURING MYOCARDIAL INFARCTION

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The literature on the treatment of cardiac arrest has been dominated by reports of open thoracotomies which often fail to mention whether simpler treatments were tried first. Zoll and others[1] and Roberts and co-workers,[2] in contrast, have stressed that a fast chest slap is the first thing to do when the diagnosis of cardiac arrest is made. The following case is presented as a confirmation of the value of that view.

Report of a Case

A 64-year-old man was brought into Sacred Heart Hospital with a severe chest pain that had begun suddenly 40 minutes before while he was playing golf. He had always been in good health, but in the previous month he had been coughing a little, with production of a small amount of yellow sputum. There had been no fever. He smoked 20 cigarettes a day.

The patient, a trim, healthy looking man, was in obvious distress, lying quietly flat on his back. He complained of a "terrible" pain deep to the center of the sternum, spreading over the entire anterior part of the chest and running down both arms to the wrists. This pain was not influenced by respiration. His color was good, respiratory rate was 16 per minute, pulse was a regular 68 beats per minute, temperature was 98 F (36.7 C) orally, and blood pressure was 150/80 mm. Hg. Heart tones were normal and the chest was clear. He was not sweating but expressed relief at the sense of coolness afforded by the oxygen tent in which he was promptly enclosed.

Morphine sulfate, ¼ grain (15 mg.), had been given intramuscularly 20 minutes before the examination of the patient. Since he stated emphatically that the pain was still increasing, another ⅙ grain (10 mg.) was given intravenously. No relief was obtained, and 20 minutes after the last injection he said that the pain was increasing even further. A few seconds later he announced suddenly, "I'm passing out," and became limp, with eyes staring. No pulse could be felt anywhere, heart tones that had been clearly heard a minute before were now absent, and there was no respiration. A diagnosis of death due to cardiac arrest was made and thoughts of immediate thoracotomy were entertained; however, the advice of Zoll[1] was recalled and three quick, heavy blows were struck on the left side of the chest with the clenched fist while the radial pulse was palpated. Just after the third blow, to my delighted surprise, a strong but very irregular pulse was felt which soon became regular. The total period of asystole was estimated to be less than a minute. About 10 seconds after the return of his pulse the patient regained full consciousness with the comment, "I must have passed out." He then vomited a large quantity of cloudy yellow fluid, afterward stating that his pain was gone and that he felt much better.

Forty minutes after the cardiac arrest his blood pressure was 120/80 mm. Hg and the pulse was regular at 64 beats per minute. The rest of his course in the hospital was remarkably smooth. He never was febrile, he did not have decompensation, and he had no more pain, except for a slight substernal twinge with coughing in the next two days.

Routine treatment with bed rest, oxygen, anticoagulants, and a restricted diet was instituted, but in addition the nurses were instructed in the manner of delivering an effective blow to the chest if the patient again collapsed.

Electrocardiograms made two hours after the onset of his pain, and 2 days, 6 days, 10 days, and seven months later, all failed to show any deviation from normal, or from each other. An hour after admission the serum glutamic oxalacetic transaminase level was 15 units, 20 hours later it was 39 units, 8 hours later it was 27 units, and five days later it was 19 units. Results of the C-reactive protein test were 4+ two days and five days after the onset of pain, but by the 12th day they were normal. The patient's hemoglobin level on admission was 13.6 Gm.%. The white blood cell count was 8,700 per cubic millimeter, with a normal differential. When this count was repeated in three days, no significant change had occurred. The sedimentation rate (Westergren) on admission was 22 and four days later was 25 mm. per hour. The blood cholesterol level the first day was 272 mg.%.

The patient was last seen seven months after the presenting illness. His electrocardiogram was identical with those obtained in the hospital. A chest x-ray was negative. He had no complaint referable to the cardiorespiratory system. He had stopped smoking as ordered, had altered his diet to reduce the animal fat content, and was continuing with a long-term program of anticoagulant therapy.

Comment

It seems reasonable to assume that this man had an electrocardiographically silent myocardial infarction and that this insult, possibly together with a distended stomach, set off the stimuli that brought about the cardiac arrest.

Parkinson and others[3] have shown that Stokes-Adams attacks in coronary thrombosis may be due to ventricular standstill, tachycardia, or fibrillation. The dramatic return of effective circulation right after the chest was struck makes it seem unlikely that any mechanism was involved except standstill.

Stephenson and co-workers[4] have shown that the chief cause of the dismal recovery rate in cardiac arrest is delay in instituting treatment. This delay stems from mental confusion in the operating room, plus the lack of simple tools at hand on the wards. It is easy to consume the vital four minutes in finding a knife, even on floors for cardiac patients, where personnel are alerted to the possibility of such a need. There is an obvious place for the chest blow in the treatment of these people while assistants gather equipment. I agree with Hosler[5] that one should not repeatedly strike the chest. If there is not an immediate response, a new approach should be taken.

As Roberts and associates[2] have pointed out, there is no reason why nurses should not be familiar with this occasionally valuable measure and exercise it, as they did in his case, with success.

Summary

A patient with cardiac arrest occurring on the ward during the painful phase of an acute myocardial infarction was successfully treated by three quick, heavy blows on the chest. It is suggested that this simple treatment be tried while equipment for resuscitation is being obtained.

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URINARY TRACT ALLERGY

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In 1922 Duke[1] described the bladder symptoms arising from food allergy and felt that this cause should be considered in those urologic patients who exhibit little or no disease in the urinary tract. He listed frequent and painful urination, bladder tenesmus, a continuous severe pain over the bladder, and polyps from allergic edema as among these symptoms and stated that "The condition may vary from slight discomfort to pain and tenesmus, which confines the patient to bed for months. Bladder allergy of long standing may be complicated by infection, in which case the symptoms of cystitis obscure the diagnosis. In patients having chronic bladder allergy no pathology may be found by internists, urologists, neurologists, roentgenologists, or pathologists, except hypersensitiveness to foods. Frequently the case may be misdiagnosed as cystitis, urethral carbuncle, misplaced uterus, or pelvic inflammatory disease. Treatment of such conditions often gives partial relief, but, as a rule, the bladder symptoms continue as severely as before." Bladder disease is frequently accompanied by generalized symptoms, including other allergic manifestations and toxemia.[2]

Although urinary tract allergy has been a recognized clinical entity for at least 37 years, the diagnosis is often missed and rarely is described in the literature. Walter[3] was able to find only four articles[4] on allergy in the *Journal of Urology* between 1940 and 1957. We feel that the possibility of

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allergy should be kept in mind in all obscure cases of cystitis, especially in persons who are otherwise allergic.

Report of a Case

A 49-year-old nun had had ragweed hay fever and asthma for 17 years. She was born in Germany and developed her hay fever seven years after coming to the United States. She was first seen in August, 1957, at which time she was treated for ragweed hay fever and asthma. The patient also had had urinary burning, dysuria, and urgency for the past 10 years, the episodes lasting two to three hours at a time and recurring at any time of the year. The attacks came about once a week and were often associated with a rash on the face and the dorsal surfaces of both hands. She was hospitalized in February, 1957, at which time tests revealed normal urine, serologic findings, and blood cell count, with 3% eosinophilis in the peripheral smear. Urine cultures yielded nonhemolytic staphylococci, sensitive to chloramphenicol (Chloromycetin) and treatment with this drug led to some lessening of her symptoms. An intravenous pyelogram showed normal findings, and cystoscopy revealed "cystitis" with generalized hyperemia of the bladder.

Physical examination revealed her to be overweight, with a pale, boggy nasal mucosa. She had a thyroidectomy scar and a cervical stump (a hysterectomy for "fibroids" had been performed in 1947); the lungs were clear and the rest of the examination normal. Laboratory studies revealed a normal nasal smear, blood cell count, and serologic findings. The basal metabolism was –4 and there were 5 to 10 white blood cells per high-power field in the urine. An electrocardiogram was normal.

Skin tests were done by both scratch and intradermal methods and revealed strong positive reactions to several ragweeds and lesser reactions to trees, grass, dust, various fungi, feathers, kapok, May flies, and pyrethrum. Food tests gave negative results by the scratch method, but intradermal testing revealed strong positive reactions to cabbage, peanuts, soybeans, and filberts. Since then the patient has received ragweed injections and has had little hay fever or asthma.

In view of the genitourinary symptoms and the positive results of the skin tests for foods it was suggested that she avoid cabbage, all members of the pea-bean family (including peanuts, soybeans, and licorice), and nuts for one to two weeks; these foods constituted a high percentage of her diet in the convent. Almost immediately her urinary symptoms cleared, and when, at our instructions, she added various of these foods to her diet her symptoms recurred. After eating nuts a blotchy eruption would appear on her face, whereas the other foods caused urinary troubles. These episodes occurred repeatedly and could always be traced to intentional or unintentional eating of these foods.

In order to eliminate the possibility of the symptoms being emotionally caused, we asked another nun to grind up some peanuts on one occasion and peas on another, and put them into the patient's food without her knowledge. Both times she developed dysuria, nocturia, and blotchiness of the face within a few minutes of the meal. The first time she reported that she had followed her diet to the letter and still had a recurrence of her urinary symptoms. The patient has been completely asymptomatic for the past eight months; she avoids the above-mentioned foods.

Comment.—Intradermal skin testing to foods is a notoriously misleading procedure, and many patients, especially children, have been almost starved because they had positive reactions on such testing. The only way one can evaluate the significance of the tests is by trial and error. A patient should avoid suspected foods for one to two weeks and then eat them one at a time at three-day intervals and in large quantities, to see if any symptoms occur. They rarely do and the patient can eat the food with impunity, ignoring the skin test. Occasionally, however, as in this case, such testing proves invaluable, for without it the proper diagnosis and treatment of a disabling condition could not have been made.

Summary and Conclusions

A case of urinary tract allergy was found to be due to various foods. The foods involved were determined by intradermal skin testing and proved by having the patient first avoid the suspected foods and then eat them on several different occasions. Reactions to intradermal skin tests of foods can be quite misleading, making dietary trials of suspected foods mandatory. The possibility of allergy should be considered in any obscure urinary tract disease.

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SPONTANEOUS ABDOMINAL PARACENTESIS

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Abdominal hernia developing as a complication of cirrhosis of the liver with ascites is a well-documented entity.[1] We recently encountered a patient with such a complication, who spontaneously perforated an umbilical hernia, resulting in a natural paracentesis. To the best of our knowledge this phenomenon has not previously been reported.

Report of a Case

The first Meadowbrook Hospital admission of this 47-year-old man, in January, 1956, was because of the development of ascites. He had a history of "moderate" alcoholic intake for many years. Pertinent physical findings at that time were a loss of chest hair, hemangiomas over the neck and scapulae areas, and extensive psoriasis. His abdomen was distended with fluid, and the liver edge was felt 3 in. below the right costal margin. The spleen was not felt. Studies of liver function revealed an indirect bilirubin level of 5.0 mg.%, cephalin flocculation 4+, alkaline phosphatase level 21 King-Armstrong units, prothrombin time 53%, and total protein level 7.0 Gm.%, with a reversal of the albumin-globulin ratio (2.6/4.4). At paracentesis 6,000 cc. of amber fluid was withdrawn. The patient was discharged on a high-protein, high-calorie diet, with vitamin supplements. He subsequently had several admissions to other hospitals for paracentesis.

He was readmitted to Meadowbrook Hospital in January, 1957, with the complaint of leakage of fluid from his abdomen. Nine months previously he had developed an umbilical hernia, which had grown progressively larger. He continued his alcoholic intake, and for several weeks had noted increasing abdominal distention and ankle edema. The night of admission he felt a trickle of fluid on his abdomen and when he investigated found fluid leaking from the hernia.

Physical examination was essentially as it had been, with the addition of a 3-cm. umbilical defect and hernia sac, leaking amber fluid. He had, in addition, developed an inguinal hernia on the left. His psoriasis was in exacerbation. The laboratory findings were as before, although the total protein level was now 5.5 Gm.%, with an albumin-globulin ratio of 3.0/2.5.

He remained afebrile, and the drainage was allowed to continue freely. Penicillin and streptomycin were given prophylactically. Three days later an umbilical herniorrhaphy was performed with the patient under local anesthesia with procaine hydrochloride and a polyethylene tube inserted through a stab wound for drainage. The postoperative course was uneventful, and the drainage continued. After the polyethylene tube was withdrawn, his abdomen began to distend with fluid. He was seen one month after discharge in the outpatient clinic, at which time his wound was well healed but his abdomen further distended with fluid. He did not return for further follow-up visits.

Comment

Abdominal hernia as a complication of Laennec's cirrhosis with ascites is a common occurrence. Snell[1a] and Chapman and co-workers[1b] found hernia to be present in 47 of 112 patients with cirrhosis, and 6 of these patients had multiple hernias, as did our patient. Henrikson[1c] reported hernia complicating 26 of 162 cases of portal cirrhosis, and Ratnoff and Patek[1d] discovered 31 of 386 patients with cirrhosis to have abdominal hernia. Umbilical hernia is the most frequent type to complicate cirrhosis with ascites; inguinal hernia is next.

External hernia results from increased intra-abdominal pressure on an area of congenital weakness of the abdominal wall. Large amounts of abdominal fluid have an effect similar to a chronic cough in the development of hernia. It is unlikely, however, that ascites is the sole etiological factor, since less than 50% of patients with massive ascites develop hernia. Altschule[2] has suggested that the hernia is present as a latent defect, which enlarges as a result of long-standing increase in intra-abdominal pressure. A further increase in intra-abdominal pressure apparently can result in perforation of a hernial sac and spontaneous paracentesis.

Our patient had been relieved of his ascites several times in the past; however, this time he waited too long. The intra-abdominal pressure rose to the height necessary to perforate the sac wall. The presence of psoriasis in exacerbation might have assisted in further weakening the sac, although there were no psoriatic lesions at the perforation site.

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COUNCIL ON DRUGS

Report to the Council

The Council has authorized publication of the following paper, which was presented as part of a symposium-panel discussion held in Washington, D. C., Sept. 25, 1958, on the Use and Abuse of Adrenal Steroids. This is the fourth paper in the series, the first three of which appeared in The Journal *on June 20 and 27 and July 4, 1959, pp. 952, 1063, and 1179.*

H. D. Kautz, M.D., *Secretary.*

STEROID THERAPY IN SKIN DISORDERS

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One of the most useful agents introduced for topical dermatological therapy in the past 20 years has been hydrocortisone (Cortef, Cortril, Hycortole, Hydrocortone) and some of its derivatives. There are currently well over 50 marketed topical preparations which contain one of these adrenal steroids. It would be a fair guess that 10 million containers of steroids were dispensed last year for the topical treatment of skin diseases, not to mention countless pills, solutions, and suspensions of steroids for oral, intramuscular, intravenous, and intracutaneous administration.

The vast majority of patients with skin diseases who receive steroids use the steroids in topical preparations. The topical use of steroids has been of great advantage. Used in this way, there are rarely any systemic side-effects, and the patient requires far less supervision than when the steroids are given orally.

As with any other disease for which steroids are used, skin diseases are controlled but not cured by these compounds. Almost without exception, use of steroids is only one of many important factors necessary to successfully manage a given skin disease. As many physicians have painfully learned, it is extremely difficult to adequately control the vast majority of skin diseases with steroids alone, even if there may be some response to steroids at some time during the disease. Unfortunately, it is still necessary to obtain a detailed history, perform extensive diagnostic procedures, and make a proper diagnosis before any attempt to use steroids can be considered. Contrary to many opinions, the introduction of steroids to dermatology has complicated rather than simplified the management of dermatoses. It is the understanding of the complexities of skin diseases which enables one to use steroids wisely to the advantage of the patient rather than to use them in ignorance to the disadvantage of the patient.

It is not the purpose of this paper to review all clinical studies that have been made on the use of steroids in skin diseases but rather to condense the results of the more exhaustive studies. Concentration will be on the use of steroids by topical application or by intracutaneous injection.

Obviously, many skin diseases, particularly the eczematous group, will respond to systemic or topical administration. Other skin diseases, such as those associated with systemic collagen diseases, pemphigus vulgaris, sarcoidosis, drug eruptions, and urticaria, may respond to systemic steroid therapy but not to topical therapy.

The great majority of reports on the clinical use of steroids by topical and intracutaneous administration have appeared in publications in the United States. They have been concerned primarily with cortisone (Cortisone, Cortogen, Cortone) acetate, hydrocortisone, fludrocortisone (Alflorone, F-Cortef, Florinef) acetate, prednisolone (Delta Cortef, Hydeltra, Meticortelone, Meti-Derm, Paracortol), and water-soluble hydrocortisone in

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various concentrations, in various vehicles, and with various added medicaments, particularly the antibiotics.

Cutaneous Absorption and Metabolism of Steroids

Paramount to understanding the action of steroids applied topically is a knowledge of how and in what quantities they penetrate the skin after they are applied to the surface. Early studies suggested that steroids were not absorbed through the skin or at least did not provoke any physiological evidence of their absorption.[1] However, it was soon clearly shown that fludrocortisone was absorbed through the skin in sufficient concentrations to give such systemic side-effects as depression of circulating eosinophils, urinary 17-ketosteroids, and urinary sodium, as well as induction of edema and weight gain.[2] Later it was shown, with tracer techniques, that hydrocortisone and cortisone were absorbed through normal skin and that, quantitatively, about 1% of the applied steroid was absorbed and excreted in the urine.[3] Malkinson[4] also demonstrated that damaging the skin by removing its superficial barrier will allow up to 75% of the steroid to pass through the skin. This variability in percutaneous absorption, which depends on the extent of cutaneous damage, explains, in part, why there is such a variation in response of given skin diseases at different times in the same person or from one person to another.

Significant contributions have been made to the problem of the metabolism and fate of steroids which are introduced into the skin.[5] Malkinson and associates have shown that the skin converts hydrocortisone to cortisone (or a very similar compound) and cortisone to hydrocortisone. Cortisone is more rapidly metabolized in skin than is hydrocortisone. Prednisone (Deltasone, Deltra, Meticorten, Paracort) and prednisolone were metabolized very slowly, if at all, after nine hours' incubation with skin.[5a] Goldman and his group have shown that water-insoluble steroids, when injected into human skin, remain in situ for extended periods of time and cause rather characteristic histological changes in the areas of injection.[6] It is known that water-soluble steroids have little, if any, clinical effect when injected intradermally, as compared to hydrocortisone. This is probably because of the rapid absorption of the water-soluble steroid from the injection site.[7]

Mode of Action of Steroids

The provocative question of "how do steroids work?" has not been answered for skin diseases any better than it has for most other diseases in which steroids have such a striking effect. There have been well over 1,000 reports concerning specific physiological and pathophysiological effects of steroids in animals and man. An excellent review has been presented by Noble.[8] However, none of these studies has given a satisfactory insight to the mechanism of action of steroids in skin diseases. Unfortunately, we are still stuck with the grossly inadequate phrase of "anti-inflammatory" to glorify our ignorance in this question.

A few of the numerous interesting effects of steroids should be included in this report because of their possible application to clinical observations. The list, which includes only a small minority of observed physiological and pathophysiological alterations induced by steroids,[9] is as follows: (1) inhibition of delayed allergic reactions; (2) in vitro inhibition of proteolytic epidermolysis; (3) inhibition of leukotoxin activity; (4) decrease in biological response to tuberculin, lepromin, iodiomycin, poison ivy antigen, histamine, Frei antigen, and Ducrey antigen; (5) atrophy of sebaceous glands (rat); (6) increased incidence of experimentally induced tumors (mice); (7) decrease in mitotic activity of the epidermis; (8) decrease in Shwartzman reaction; (9) suppression of anaphylaxis; (10) antipyretic activity; and (11) depression of the basic inflammatory response, i. e., decrease in vasodilatation, stickiness of cells to vessel wall, diapedesis, and exudate. Despite such fundamental observations and the phenomenal versatility of steroids in altering physiological functions, there is no solid base for explaining the mechanism of action of steroids in skin diseases.

Clinical Use of Steroids

The first consideration in the clinical use of steroids in skin diseases is to determine what diseases are improved by their use and in what form (oral, intracutaneous, topical) they are used to best advantage. The table summarizes many reports in an attempt to outline the answer to this question.[10] Obviously, for most of these skin diseases, other therapeutic measures are as important or even more important in their management.

Most skin lesions that respond to topical application of steroids will also respond to oral or intracutaneous injection of the steroid. However, many skin diseases which respond to oral or intracutaneous administration will not respond to topical application. There are some skin lesions which will respond to intracutaneous injection of steroids but not to either oral or topical use. For the most part, these differences are best explained on the basis of concentration of the steroid in the area in which it is needed. The concentration needed locally, if attained by systemic administration, will usually lead to severe systemic complications if continued over a prolonged period of time. Intracutaneous use has led to practically no systemic complications because of the concentration of this form of therapy on small lesions. However, intracutaneous injection may lead to local atrophy or even sensitization by an ingredient in the suspension other than the steroid.[10v] These complications are reversible and with due caution should not seriously interfere with the judicious use of steroids administered intracutaneously.

Some workers have shown that mild systemic side-effects are possible from the topical use of fludrocortisone. However, systemic effects from topical use of hydrocortisone or prednisolone, even over large areas for long periods of time, are practically nonexistent.

The danger of local infection in areas treated topically with steroids is minimal, except for herpes simplex, which may spread alarmingly in the presence of steroid therapy. It has been somewhat surprising to dermatologists that secondary infection induced by steroid therapy has been so rare, particularly in view of the warnings that were initially given after experience with severe spreading bacterial lesions provoked in other organs by the systemic administration of steroids.

The use of antibiotics incorporated in steroid ointments and lotions as a preventive measure seems to have but little justification in the vast majority of cases. If a skin disease for which a topically administered steroid is indicated is secondarily infected, it would seem wise to treat the lesion with a steroid combined with an antibiotic.[10w]

In spite of the large number of reports on the topical use of various steroids, there are relatively few experiments which are well controlled throughout. The studies which have been carefully done indicate that hydrocortisone is as good as any of the steroids, if not superior to them.[11] Fludrocortisone, in one-tenth the concentration of hydrocortisone, is probably as effective as hydrocortisone[12] but does have the remote yet definite disadvantage of systemic side-effects.[10o] Water-soluble hydrocortisone seems to be as good as water-insoluble hydrocortisone,[13] and prednisolone may be slightly inferior to hydrocortisone.[14] These different steroids are used in variable concentrations, which may partly explain slight variations in effect among hydrocortisone, fludrocortisone, water-soluble hydrocortisone, and prednisolone. New derivatives of steroids are now being tested for their topical effects in skin diseases. As yet there is no definite evidence that they are superior to those mentioned previously.

In general, the higher the concentration of the steroid at its application site the more beneficial it will be. Frequently, the difference in response between a 1% and a 2.5% concentration of hydrocortisone is not significant enough to justify the added expense. The same fundamental also applies to intralesional injection of steroids. It is wise to use the smallest possible concentration of steroids intracutaneously because of the unpleasant complication of atrophy of the skin at the injection site with higher concentrations. It might be added that cortisone is useless when applied topically,[15] but it is fortunate that topical steroid therapy was not abandoned on the basis of this initial experience.

The base in which the steroid is incorporated seems to make some difference in therapeutic effect.[16] In general, the bases used are primarily three types: (1) greasy or hydrophobic, (2) creams or hydrophilic, (3) lotions. In wet, oozing lesions the lotions are more satisfactory, and in intertriginous areas the creams and lotions are more satisfactory than the greasy bases. However, for most skin lesions in most areas the hydrophilic bases seem slightly superior. It is difficult to state any generalities about choice of a base, and it usually requires the intuition of an experienced dermatologist to pick the right type of base for any given lesion.

More steroids applied topically are probably used in treating eczematous diseases of the skin than all the other skin diseases combined. This is understandable when one considers that about 25% of all patients treated by dermatologists have an eczematous disease and that most of the eczematous diseases are improved by the topical use of steroids. There is some debate as to whether steroids applied topically are of any value in allergic contact dermatitis.[17] In severe cases, certainly, the oral use of steroids has a dramatic effect. The greatest benefit of the topical use of steroids in eczematous eruptions probably is experienced in atopic dermatitis and related diseases such as infantile eczema, dyshidrosis, housewife's eczema, and neurodermatitis. The topical use of steroids alone is hardly worthwhile, however, unless the other important therapeutic factors in this disease group are incorporated in the treatment regimen. Long-term topical use of steroids in most of the eczematous diseases has real advantages; however, this means daily application of steroids for many weeks and even months after visible signs of the disease have disappeared.

The oral use of steroids in eczematous diseases should be discouraged as much as possible. These diseases are chronic, recurrent, and persistent. Prolonged management with steroids given orally frequently leads to unpleasant, if not drastic, side-effects. Usually the dose level for control of the disease increases as time goes on. All too frequently, after two to three years of oral steroid therapy, the physician has to tell his scratching, eczematous, unhappy "Cushingoid" patient that the oral medication must finally be stopped and that he must now try to get along on steroids applied topically and other forms of management. Too many such patients are given oral steroid therapy for the following unjustifiable reasons: (1) to impress the patient with a dramatic initial response, (2) to obviate having to explain the details of the disease to the patient and the complicated factors in its course and management, and (3) because of ignorance of the other important and effective methods of control of this disease group. Only the most severe, extensive, and recalcitrant eczematous eruptions present occasional legitimate grounds for the oral use of steroids.

Uses of Adrenal Steroids in Skin Diseases

	Route of Administration		
	Oral	Intracutaneous	Topical
Disease	Response*		
Alopecia areata	Good	Good	None
Anogenital pruritus	Good	Good	Good
Atopic dermatitis	Good	Good	Good
Chondrodermatitis nodularis chronica helicis	...	Good	None
Contact dermatitis	Good	Good	?
Dermatitis herpetiformis	Good	...	None
Dermatomyositis	?	...	None
Drug eruptions	Good	...	None
Erythema multiforme	Good	...	None
Granuloma annulare	...	Good	None
Kaposi's sarcoma	None	...	...
Lichen planus	?	Good	None
Lichen vidal	?	Good	?
Localized myxedema	...	Good	None
Lupus erythematosus	Good	Good	None
Lymphomas	Good	Good	None
Mycosis fungoides	Good	Good	None
Necrobiosis lipoidica diabeticorum	...	Good	None
Nummular eczema	Good	Good	Good
Pemphigoid	Good	...	None
Pemphigus vulgaris	Good	...	None
Periarteritis nodosa	Good	...	None
Pityriasis lichenoides et varioliformis acuta	Good	...	None
Postherpetic neuralgia	?	...	None
Psoriasis	?	Good	None
Pustular bacterid	...	...	None
Pyoderma gangrenosum	?	...	None
Sarcoidosis	Good	Good	None
Scleroderma	?	...	None
Solar urticaria	None	...	None
Synovial cysts	...	Good	None
Urticaria	Good	...	None
Xanthoma	...	Good	None

* ... = Insufficient data; ? = variable response.

There is a justifiable growing interest in the use of steroids in suspension for intracutaneous injection. This method, of course, is confined to relatively small lesions which are few in number. Examples of such lesions in which intracutaneous administration of steroids presents real advantages are sarcoidosis, necrobiosis lipoidica diabeticorum, granuloma annulare, lichen vidal, synovial cysts, xanthomas, keloids, localized myxedema, resistant plaques of discoid lupus erythematosus, and hypertrophic lichen planus (see table). Most interesting is the realization that such a large number of dermatoses can be suppressed by steroids if the local concentration is high enough. One hopefully awaits the topically applied steroid which will pass easily into the skin and remain in the skin for prolonged periods of time.

Orally administered steroids have been extremely useful in managing acute urticaria, various drug eruptions, pemphigus vulgaris, pemphigoid, and erythema multiforme. Steroids given orally will regrow hair in alopecia areata, but they should be given only to highly selected cases, if at all. It is generally agreed that disseminated lupus erythematosus and periarteritis nodosa are dramatically controlled, as a rule, with orally administered steroids, but other diseases of the "collagen disease group" such as scleroderma and dermatomyositis have not responded particularly well to oral administration.

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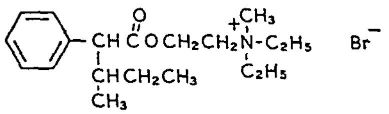
NEW AND NONOFFICIAL DRUGS

The following descriptions of drugs are based upon available evidence and do not in any case imply endorsement by the Council.

H. D. Kautz, M.D., *Secretary.*

Valethamate Bromide (Murel).—2-Diethylaminoethyl 3-methyl-2-phenylvalerate methylbromide.—The structural formula of valethamate bromide may be represented as follows:



Actions and Uses.—Valethamate bromide, introduced in 1958, is a quaternary ammonium compound which is used clinically as an antispasmodic. Animal experiments indicate that the drug acts predominantly as an anticholinergic agent. In addition, it exerts a mild direct inhibiting effect on the motility of smooth muscle. Valethamate is also said to exhibit a transient ganglionic blocking action; such effects are minimal, if not imperceptible, in the doses used clinically. The drug does not diminish gastric secretion to any appreciable extent.

Valethamate bromide is proposed for oral and parenteral use for the treatment of hypermotility and spasm of the gastrointestinal, genitourinary, and biliary tracts as well as for the adjunctive management of peptic ulcer. Although favorable results have been reported in some patients, the bulk of the clinical evidence available to date is uncontrolled and is based on subjective rather than objective observations. Further studies under controlled conditions are indicated before the efficacy of valethamate can be fully assessed.

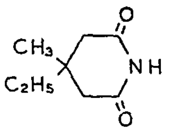
In the usual doses employed clinically, typical anticholinergic side-effects have not been frequent. At higher doses, such effects as dryness of the mouth, blurring of vision, circulatory disturbances, and interference with micturition or defecation have occurred. On the basis of its anticholinergic classification, valethamate should be used cautiously in the presence of glaucoma, organic pyloric stenosis, prostatic hypertrophy, or urinary retention.

Dosage.—Valethamate bromide is administered orally, intramuscularly, or intravenously. Dosage so far employed has been variable. For mild to moderate spasm of the gastrointestinal, genitourinary, or biliary tracts and for peptic ulcer, the proposed oral dose ranges from 10 to 20 mg. three or four times daily. For acute spasm and for severe symptoms of peptic ulcer, the drug is proposed for intramuscular or intravenous injection in doses ranging from 10 to 20 mg. every four to six hours. Pending more conclusive evidence to show a beneficial effect, the foregoing dosages are considered experimental.

Preparations: solution (injection) 50 mg. in 5 cc.; tablets 10 mg.

Ayerst Laboratories, Division of American Home Products Corporation, cooperated by furnishing scientific data to aid in the evaluation of valethamate bromide.

Bemegride (Megimide).—3-Ethyl-3-methylglutarimide.—The structural formula of bemegride may be represented as follows:



Actions and Uses.—Bemegride, introduced in 1954, should be regarded as a central nervous system stimulant, most appropriately categorized as an analeptic. Although the drug was introduced with the thought that it might prove to be a specific antagonist to barbiturates, it was found to antagonize the action of other depressants as well, and the conception that its action is in any way specific for barbiturates has been abandoned. Apart from its general effect on the central nervous system, no evidence is available to indicate that bemegride possesses any other pharmacodynamic properties when given in the dosage used clinically.

Clinical interest in bemegride centers chiefly upon its use in barbiturate intoxication, although it has also been employed after thiopental anesthesia to lessen the depth of anesthesia and hasten recovery. Several reports have described its use in glutethimide poisoning. Its action in the presence of central depression by other drugs has had only limited clinical investigation.

The use of bemegride in barbiturate poisoning may result in improved muscle tone, a return or increase in reflex activity, spontaneous movements, increase in respiratory rate and minute volume, elevation of the blood pressure, and lessening of the depth of coma. It apparently neither accelerates the elimination of barbiturates from the body nor induces awakening at higher barbiturate blood levels. Whether its use improves the prognosis for ultimate recovery is part of the highly controversial question of the value of any analeptic in barbiturate intoxication. Certainly, the use of bemegride or other analeptics is to be regarded as an adjunct to other therapeutic measures, especially maintenance of a patent airway, artificial respiration, and administration of oxygen. (See the general statement on central nervous system stimulants and the monograph on picrotoxin in New and Nonofficial Drugs.)

Response to bemegride is prompt. Effects of intravenous injection in unanesthetized animals are manifested almost immediately. On the other hand, in the presence of barbiturate-induced coma, a series of injections, given according to the schedule outlined later, may be necessary before optimal stimulation is produced. Furthermore, once optimal stimulation from bemegride has been achieved, complete recovery of the patient may not ensue for an additional eight hours or more. Since the effects of bemegride are frequently transitory, the patient should be watched carefully for signs of regression. Should this occur, a further series of bemegride injections may be given if desired.

The effects of overdosage of bemegride closely resemble those of other analeptics. In unanesthetized mice, toxic doses produce jerks, spasms, hyperpnea, the Straub tail phenomenon, followed by clonic and tonic convulsions and death. In human patients depressed by barbiturates, bemegride may produce hyperactivity of reflexes, muscular twitching, and convulsions. Retching and vomiting are said to be the earliest signs of incipient toxicity. A delayed psychotic reaction characterized by lability of mood, euphoria, confusion, and visual hallucinations, is reported to have occurred in patients reawakening from barbiturate intoxication after treatment with bemegride. Since, however, similar symptoms have also appeared in patients treated with other analeptic agents and in those to whom no analeptic agents were administered, there is little reason to regard the syndrome as a specific consequence of bemegride therapy. No reports of serious chronic toxicity have appeared.

A final assessment of the relative merits of bemegride in comparison with other analeptics must await further clinical study. At present, it may only be suggested that, although bemegride is a useful addition to the list of analeptics available, this agent has not yet been established as clearly superior to certain older drugs of the group.

Dosage.—Bemegride is administered intravenously. In acute barbiturate poisoning, a fixed dose cannot be stated, since the amount required will depend on the degree of depression as well as on other factors, necessitating careful evaluation of the individual patient. With the patient under continuous observation, doses of 50 mg. may be injected at intervals of three to five minutes until there are clinical signs of improvement or until signs of toxicity intervene.

When used to decrease the depth of barbiturate-induced surgical anesthesia, 50-mg. doses of bemegride are injected on a similar schedule; here a single such dose may be sufficient, although as many as two to four injections may be required.

During bemegride therapy, it is advisable to have at hand a solution of a short-acting barbiturate for intravenous injection for possible use should dangerous manifestations of overdosage appear.

Preparations: solution (injection) 50 mg. in 10 cc.

Abbott Laboratories cooperated by furnishing scientific data to aid in the evaluation of bemegride.

THE MULTIPLE TRANSFUSION DANGER.—With the broadening scope of radical surgical procedures dependent upon the availability of large amounts of blood for tranfusion, there has developed a dangerous hemorrhagic complication which, because of its insidious onset, has been inadequately appreciated. . . . Review of the records for the past 18 month period at Saint Joseph Hospital, [Burbank, Cal.], revealed 24 instances in which patients had received ten or more units of blood within a relatively short period of time. . . . Six of these patients (25%) developed manifestations of a hemorrhagic diathesis. . . . The blood clotting mechanism is a complex chemical system represented by a large number of blood factors dependent on each other in proper concentration for integrated action in providing blood coagulation when needed, but held in delicate balance by antagonistic anticoagulating and fibrinolytic systems. Disturbance of the concentration of any of these factors, or stimulation of the anticoagulating or fibrinolytic systems by any cause, therefore, may result in a hemorrhagic diathesis. It should be borne in mind that prior to surgery, patients may have an occult disturbance of the blood clotting mechanism, either congenital or acquired, and any of the mechanisms . . . that would further disturb the balance of blood clotting, could readily convert a potential hemorrhagic diathesis into an active one. . . . When more than five units of stored blood are to be given in rapid succession, provision should be made to have fresh blood (less than four hours old) available. It would be preferable to give direct transfusions of whole blood. In the event that fresh blood is not available, it is suggested that one gram of calcium, either as the chloride or gluconate, be given intravenously for every two units of citrated blood. Such supplemental medication must not be injected into the bottle of citrated blood being administered.—R. Straus, M.D., W. T. Sweeny, M.D., and D. Plotkin, M.D., The Multiple Transfusion Danger, *Western Journal of Surgery, Obstetrics and Gynecology,* March-April, 1959.

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IS THERE A CORTICOSTEROID OF CHOICE FOR RHEUMATOID ARTHRITIS?

GUEST EDITORIAL

L. Emmerson Ward, M.D.

CURRENTLY more than 125 different types of tablets containing an antirheumatic steroid are being sold in the United States. Thus, it is apparent that one of the early problems in the use of cortisone, that of supply, has been solved. However, the solution has created a new problem. In this issue of THE JOURNAL (page 1253) Neustadt appropriately calls attention to the doctor's current dilemma, arising from competitive advertising claims and conflicting medical reports, namely, the selection of an antirheumatic steroid for his patient with rheumatoid arthritis.

Seven different cortisone-like drugs, in addition to corticotropin, are now commercially available for, and commonly used in, the steroidal treatment of rheumatoid arthritis. All seven have qualitatively similar antirheumatic effects; however, they differ notably in certain other characteristics.

Cortisone, currently the least costly, has the additional advantage of the longest period of use. Hydrocortisone exhibits antirheumatic and metabolic effects of about the same kind and order as those of cortisone, but is perhaps slightly more potent. Allowing for this small and inconstant difference in potency, there seems to be little or no difference in the systemic effects of these two hormones; equivalent antirheumatic doses produce similar physiological effects. However, hydrocortisone has proved superior to cortisone in local use; for example, intra-articularly. Hydrocortisone apparently is the chief product of the normal human adrenal cortex; presumably corticotropin exerts its antirheumatic effect chiefly by stimulating the adrenocortical secretion of hydrocortisone.

Prednisone and prednisolone differ structurally from cortisone and hydrocortisone only in the presence of a double bond between the first and second carbon atoms of the steroid molecule. This slight alteration invests these two compounds with an approximately fivefold increase of antirheumatic potency, and unfortunately with a similar increase in the so-called glucocorticoid metabolic activity, when these compounds are compared to cortisone, milligram for milligram. The effect on electrolytes, however, is not increased. Thus, although antirheumatic doses of these compounds equivalent to those of cortisone or hydrocortisone cause less loss of potassium, retention of sodium, and edema, nevertheless they have just as great a tendency to produce the other undesired metabolic effects. The systemic actions of prednisone do not differ significantly from those of prednisolone.

Methylprednisolone seemed to possess a greatly enhanced anti-inflammatory potency and relatively less metabolic activity in animals. When administered to patients who had rheumatoid arthritis, however, it proved to be generally similar to prednisone and prednisolone. Although some investigators have reported that methylprednisolone has a slightly more potent antirheumatic effect than prednisolone and that it produces less edema and fewer of certain other undesired effects, others have found that it has little or no significant advantage over prednisone or prednisolone. Methylprednisolone is neither the first nor the last analogue of cortisone known to affect animals and man differently. Indeed the greater the alteration of the structure from that of the naturally occurring adrenocortical hormones, the greater this disparity generally seems to become. Thus, while investigations on animals provide invaluable screening information, they do not predict accurately the effect of antirheumatic steroids on man.

Triamcinolone also is about equal to prednisone in antirheumatic activity and in most metabolic effects according to many investigators; it is slightly more potent according to others. That it is a significantly better steroid for the treatment of rheu-

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From the Section of Medicine, Mayo Clinic and Mayo Foundation, Rochester, Minn.

matoid arthritis has not been established, but it does have several noteworthy characteristics. It has little tendency, perhaps the least of currently available antirheumatic steroids, to produce mental stimulation or to cause retention of sodium and edema. Triamcinolone, according to some investigators, causes fewer gastrointestinal symptoms than do other analogues of cortisone. However, peptic ulcers have developed during treatment with this compound; whether it will prove to be less ulcerogenic than its competitors remains to be determined. Triamcinolone causes anorexia and loss of weight in some patients, in contrast to the usually opposite effect of other antirheumatic steroids. An unusual degree of muscular weakness and wasting and erythema of the skin and other vasomotor phenomena have developed occasionally in patients taking triamcinolone.

Dexamethasone, the newest of the analogues of cortisone, is also the most potent, milligram for milligram. Its antirheumatic strength and metabolic effects are approximately seven times those of prednisone. That it has a significant therapeutic advantage over some of its predecessors has not yet been demonstrated. Clinical experience with it, however, is relatively limited and more information is needed concerning results of prolonged usage and concerning certain of its properties such as its effects on the central nervous system, on appetite and weight, on electrolytes, on the formation of edema, on excretion of calcium, and on metabolism of carbohydrates.

Which steroid is best for rheumatoid arthritis? Clinically, some patients seem to fare a little better on one compound, others on another. Certain physicians prefer this steroid, others that. The introduction of each new antirheumatic steroid has been followed by initial enthusiasm during which time the new compound has been hailed by some as showing relatively fewer undesired metabolic effects for a given antirheumatic effect. Experience has shown, however, that considerable time, perhaps several years, is required before the effects of an antirheumatic steroid in the prolonged treatment of a disease such as rheumatoid arthritis can be evaluated properly. And as each new steroid has been used longer and more extensively, its apparent therapeutic efficacy, at least in terms of the more significant metabolic effects, has seemed to approach that of its predecessors. Accurate comparison of the antirheumatic and the metabolic activities of cortisone-like steroids in patients is a difficult, exacting, and time-consuming procedure. Yet many more comparative studies, such as those reported by Neustadt and carried out for even more prolonged periods, are highly desirable.

No one steroid as yet has demonstrated convincing superiority over all its competitors in all, or even in a majority of, patients with rheumatoid arthritis. Generally, the best steroid for treatment of rheumatoid arthritis today is that which is administered by the physician who selects his patient properly, supplements steroidal therapy with other appropriate measures of treatment, supervises the administration of the drug carefully, and regulates the dosage to achieve a reasonable antirheumatic effect with avoidance of, or a minimum of, undesired effects. Wise usage is of more importance than the particular steroid administered.

Increased potency, in itself, is of no particular practical importance. Of significance, however, is the dissociation of antirheumatic effects from undesired metabolic effects. This has been achieved to a remarkable degree in respect to effects on electrolytes by several of the newer analogues of cortisone, but unfortunately the same has not been accomplished in respect to other metabolic activities which pose much greater problems during prolonged administration. Whether the antirheumatic effect can be dissociated from these other metabolic effects remains to be demonstrated. However, in this age of accomplishment that which seems doubtful or impossible today often will have been achieved by tomorrow.

Pharmaceutical companies at times have been criticized for overenthusiastic advertising of cortisone-like steroids and of other drugs by their sales departments. However, such criticism must be tempered with admiration for the splendid (and costly) achievement in biochemistry, medical research, and pharmaceutical technology which the introduction of a new steroid represents. Likewise, the antirheumatic steroids generally should be blamed less for their imperfections and credited more for their virtues and for the encouragement that even better compounds eventually will be forthcoming.

CHANGE OF ADDRESS

If you change your address please notify The Journal at least six weeks before the change is made. Include the address label clipped from your latest copy of The Journal, being sure to clearly state both your old and new address. If your city has Postal Zone Numbers, be sure to include this Zone Number in your new address.

ORGANIZATION SECTION

LETTER TO SUBCOMMITTEE ON IMMIGRATION AND NATURALIZATION

May 26, 1959

Hon. James O. Eastland, Chairman
Subcommittee on Immigration and Naturalization
Senate Office Building
Washington 25, D. C.

Dear Mr. Chairman:

It is the understanding of the American Medical Association that your Subcommittee is currently considering a number of amendments to the Immigration and Naturalization Law. The purpose of this letter is to submit, for the consideration of the Subcommittee, the position of the Association on one phase of this law.

We understand that the Subcommittee is concerned with the possibility of extending or making permanent certain provisions of Public Law 85-316. We are particularly concerned with those provisions of the law which permit orphans and others afflicted with tuberculosis to be admitted to permanent residence in the United States and with the provisions that authorize the proxy adoption of orphans. With respect to tubercular orphans, it is our understanding that the regulations established by the United States Public Health Service have resulted in the protection of both the child and the adoptive families and his community. Of more than 1100 children brought in under that provision only six have become subject to deportation procedure because of refusal to comply with the regulation.

On the other hand, it is our understanding that the law does not provide for regulations to control the admission of children adopted by proxy. As a result, some of these children have arrived in the United States suffering from pneumonitis, scabies and other contagious diseases.

In order to protect not only the child but his adoptive parents and the community, the American Medical Association urges the Subcommittee to amend the law so as to provide authority for the Attorney General to prescribe regulations, after consultation with the United States Public Health Service and other agencies of the Department of Health, Education and Welfare, which would preclude, temporarily, the issuance of visas, both quota and nonquota, for persons suffering from serious illnesses other than those which would exclude them under existing law. The purpose of this amendment would be to give to the United States Public Health Service authority to make recommendations concerning the issuance of visas to individuals suffering from acute conditions at the time of their departure for the United States.

The House of Delegates of the American Medical Association at its meeting in San Francisco in June, 1958, adopted a resolution embodying these principles. This position was reiterated by the House of Delegates at its meeting in Minneapolis last December.

The Association believes that those persons who have opened their homes to Korean orphans should be highly commended. It is our hope that those who have undertaken the task of transporting these unfortunate children to new homes will continue their work. It is our belief, however, for the reasons mentioned above, that more stringent health controls are necessary.

On behalf of the Association I would like to thank you for this opportunity to present our views and to assure your Committee of our willingness to provide whatever additional assistance in connection with this problem that you desire.

Sincerely yours,
F. J. L. BLASINGAME, M.D.
Executive Vice-president.

QUARTERLY CUMULATIVE INDEX MEDICUS

Volume 60 (July-December 1956) of the Quarterly Cumulative Index Medicus is now available and may be ordered from Mr. Kroeger, Circulation and Records Department. This will be the final volume of the Index.

NEW A. M. A. PUBLICATIONS

A new A. M. A. leaflet entitled "As Others See Us," published by the Joint Committee on Health Problems in Education of the National Education Association, was written primarily for teen-agers. This illustrated, easy-to-read leaflet will prove valuable to doctors, educators, ministers, parents, and youth counselors for the insight it provides into the problems of adolescence. The cost of a single copy is 25 cents; quantity discounts are available.

"Old King Cold" is a shirtpocket-sized pamphlet containing suggestions that can help employees avoid the common cold, hasten recovery, and prevent complications. The cost of a single copy is 15 cents; quantity discounts are available.

These publications may be purchased from the Order Department, American Medical Association, 535 N. Dearborn St., Chicago 10.

COUNCIL ON MEDICAL EDUCATION AND HOSPITALS

LIMITS ON STAY OF EXCHANGE VISITORS

The Department of State, Washington, D. C., has issued the following notice to responsible officers of exchange-visitor programs.

In the administration of the Exchange-Visitor Program authorized by the United States Information and Educational Exchange Act of 1948, the Department has noted that many exchange visitors are attempting to remain in the United States longer than is necessary for purposes of the program. Such attempts are contrary to the intentions of the Congress of the United States, which based the exchange visitor program on the concept that the exchange visitor would return to his homeland to foster abroad a better understanding of our way of life. To meet the problem the Department of State and the Immigration and Naturalization Service have set the following general limits on the stay of exchange visitors.

1. Graduate nurses will be limited to a stay of two years.
2. Doctors of Medicine will be limited to a stay of five years for internships and residencies.
3. Students will be permitted to remain as long as they pursue substantial scholastic programs leading to recognized degrees or certificates and show clear progress toward earning the degrees or certificates. Students whom the sponsoring schools recommend for practical training should be permitted to remain for such purpose up to 18 months after receiving their degrees or certificates.
4. Research scholars will be limited to a stay of three years.
5. Guest teachers and instructors will be limited to a stay of two years.
6. Business and industrial trainees will be limited to a stay of 18 months.

These limits apply to present and future exchange visitors. They apply regardless of the number of programs in which an exchange visitor participates; this means that a transfer from one program to another will not extend the limits of the stay of exchange visitors beyond the limit set for the particular category of exchange visitor. These limits should not be construed as changing any limit specified in the official description of a program.

GOVERNMENT SERVICES

AIR FORCE

Space Age Display.—The space age display showing the latest research projects under way at the Air Force School of Aviation Medicine won a certificate of achievement for the best display in the military medicine section at the Atlantic City meeting in June. The exhibit showed the progress in such areas of space medicine research as weightlessness, closed systems which produce oxygen photosynthetically, and sealed space cabin simulator experimentation.

VETERANS ADMINISTRATION

Personal.—Dr. Samuel H. Bassett, assistant director of professional services for research at the Veterans Administration center in Los Angeles, and Dr. Edward D. Freis, chief of the medical service at the Mount Alto (Washington, D. C.) VA Hospital, were appointed the agency's first senior medical investigators. In their new senior research positions, these physicians will remain at their VA hospitals to apply their research skills full time to health problems of greatest importance to veterans. The new VA senior investigator program will for the first time permit VA doctors to engage in full-time research. Nearly all VA medical research is done by the agency's regular hospital and clinic personnel as a voluntary activity in addition to their clinical duties. The senior investigators may hold appointments to the staffs of colleges and universities on a nonsalary basis and have VA teaching and patient-care repsonsibilities to the extent of not more than 25% of their working time.

PUBLIC HEALTH SERVICE

New Hazards from Plastic Bags.—The Public Health Service made an intensive study of 10 cases of suffocation in infants and children involving plastic bags. Only one of the deaths so far investigated was caused by a child pulling a bag over his head. In six cases, plastic dry cleaning bags used as improvised mattress covers, pillow covers, or blanket protectors were the cause of suffocation, the infant either pulling the plastic against its face or lying face down on a bed covered with a plastic dry cleaning bag. The study, which included autopsies in six cases, revealed no evidence of respiratory infections. The absence of such evidence indicated that the deaths were caused by mechanical suffocation. The Public Health Service has alerted all health departments to the need for public education on the dangers of misusing plastic materials and has endorsed an educational pamphlet which is being widely distributed by the Society of the Plastics Industry.

MEDICAL NEWS

CALIFORNIA

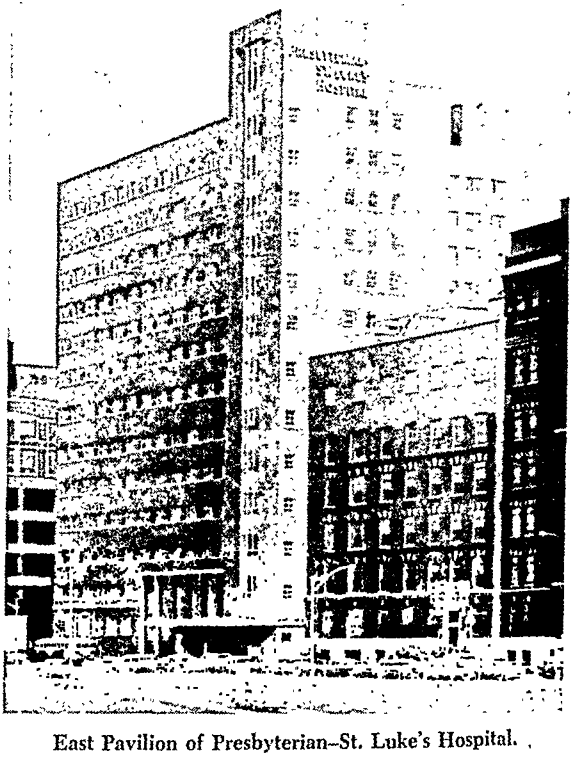
Korean Receives First Doctorate in Biostatistics.—On June 11 at the University of California, Berkeley, a Korean physician, Dr. Chai Bin Park, received the first doctorate in public health in biostatistics in the history of the University of California. Dr. Park came to the University of California in 1955 under a fellowship from the American-Korean Foundation to study for the degree of master of public health which he received in June, 1956. Since then Dr. Park has supported himself through fellowships and teaching assistantships. He is returning to Korea on passage provided by the American-Korean Foundation in July. The American-Korean Foundation, a permanent organization founded in 1952 "to help the Koreans help themselves," has brought 130 Korean physicians to the U. S. for advanced training.

ILLINOIS

Chicago

Deed for Medical School Development.—Governor William G. Stratton and Dr. Walter H. Theobald, president of the Medical Center Commission, turned over the deed to about 10 acres of land in the Medical Center District on Chicago's West Side to Dr. John J. Sheinin, president, Chicago Medical School, June 4. This is a further step in the realization of the school's development program which provides for the construction of educational, research, and other facilities to replace the present four-story building at 710 S. Wolcott Ave. The new campus will be bounded by Harrison and Polk Streets, Damen, Ogden, and Hoyne Avenues. According to Dr. Sheinin, the first four buildings being planned include a medical research institute, a new medical school building, and student and faculty dormitories. Construction of the 10-story, block-long, research institute will cost over 4 million dollars. A grant in the amount of $1,121,000 has already been received for this building from the U. S. Public Health Service. The 17-story medical school building will cost over 7 million dollars including the equipment, and the dormitory buildings will cost about 2 or 3 million dollars each. The cost of the entire project, land included, is estimated at 25 million dollars. The Chicago Medical School currently enrolls about 72 students each year. In the new school it is planned to enroll 100 each year. In addition to the four-year medical course, a graduate school is planned for students working for advanced degrees.

Complete Hospital Merger.—The complete physical merger of Chicago's Presbyterian and St. Luke's Hospitals in the city's West Side Medical Center was accomplished by July 1. The two institutions were merged in 1956, and their combination into the new *Presbyterian-St. Luke's Hospital* has created an institution with a bed capacity of 900. The new hospital is the only private, voluntary, nonprofit hospital in the West Side Medical Center. It is affiliated with the University of Illinois College of Medicine in the Medical Center and is an integral part of the university's teaching program. Presbyterian-St. Luke's new 13-story Pavilion of 490 beds was completed last summer and at present a Medical Science Research Building is under construction. Scheduled for completion in March, 1960, this building primarily will house laboratories and surgical suites.



East Pavilion of Presbyterian-St. Luke's Hospital.

Physicians are invited to send to this department items of news of general interest, for example, those relating to society activities, new hospitals, education, and public health. Programs should be received at least three weeks before the date of meeting.

IOWA

Dr. L. A. Coffin Memorial Fund.—To perpetuate the memory of the first Iowan to be chosen by the A. M. A. as its "General Practitioner of the Year," friends of Dr. L. A. Coffin established a fund in his name from which loans can be made to medical students who offer some assurance that they will enter the general practice of medicine. Inasmuch as Dr. Coffin was one of the founders of the Educational Loan Fund of the Iowa State Medical Society, the Dr. L. A. Coffin Memorial Fund is to be administered by the officers of the fund, and the rules governing disbursements and repayments are to be identical for the two, with the single exception that has been mentioned. Those who wish to make gifts to this establishment should draw their checks to the Dr. L. A. Coffin Memorial Fund and send them to the office of the State Medical Society, in Des Moines.

KENTUCKY

Dr. Lacovara Honored.—On June 5 Dr. Dominick J. Lacovara, Ashland, was presented with the Tristram Walker Metcalfe Alumni Award at Long Island University in New York. The award, a mahogany plaque with bronze lettering, is given to perpetuate the memory of Long Island University's first president, Tristram Walker Metcalfe. The presentation speech cited Dr. Lacovara "for unceasing efforts to probe criminal behavior, for his work in the rehabilitation of offenders, for serving society and for his extensive lecturing on mental health and juvenile delinquency."

LOUISIANA

Fall Session on Pediatrics.—The Louisiana Chapter, American Academy of Pediatrics, will present a fall scientific session under the sponsorship of Lederle Laboratories, with the Baton Rouge Pediatric Society as host, Friday, Sept. 18, at the Capitol House, Baton Rouge. The theme of the seminar will be "Malignancies in Childhood" and will include the following subjects and speakers:

Common Childhood Tumors, Dr. James B. Arey, Philadelphia.
Malignancies of the Endocrine System, Dr. Robert B. Greenblatt, Augusta, Ga.
Abdominal Masses in Children, Dr. H. William Clatworthy Jr., Columbus, Ohio.
Radiologic Diagnoses of Childhood Malignancies, Dr. Frederic N. Silverman, Cincinnati.
Advances in Treatment of Blood Dyscrasias, Dr. Wolfgang W. Zuelzer, Detroit.
Chemotherapy of Malignancies, Dr. John R. Heller, Bethesda, Md.

There will be two round-table discussions with Dr. James P. King, St. Louis University, as moderator. At the noon banquet, Dr. John G. Young, clinical professor of pediatrics, University of Texas Southwestern Medical School, Dallas, will speak on "Emotional Problems of Parents and Children." Other week-end activities in Baton Rouge Sept. 19 include a breakfast meeting of the Louisiana Chapter, American Academy of Pediatrics, and the Sixth District Medical Society meeting. For information, write Dr. Francis M. Harris Jr., Secretary-Treasurer, 1401 N. Foster Dr., Baton Rouge 6, La.

MICHIGAN

Public Health Specialists Retire.—Three public health specialists, Henry F. Vaughan, Dr. P. H., first dean of the School of Public Health, Pearl L. Kendrick, Sc.D., who pioneered in the prevention of whooping cough at laboratories in Grand Rapids, and Mr. Walter D. Tiedeman, authority on food and milk control, retired in June from the University of Michigan, Ann Arbor. The three were honored at a dinner June 6. Earlier, representatives of four Michigan Sanitarian Associations presented Dr. Vaughan and Mr. Tiedeman with "scrolls of appreciation for their contributions to the field of environmental health."

MINNESOTA

State Medical Election.—The officers elected at the 1959 annual meeting of the Minnesota State Medical Association are: president-elect, Dr. Clarence Jacobson, Chisholm; first vice-president, Dr. William E. Macklin, Willmar; second vice-president, Dr. Gordon J. Strewler, Duluth; secretary, Dr. Brian J. McGroarty, 738 Lowry Medical Arts Bldg., St. Paul 2; treasurer, Dr. Karl W. Anderson, Minneapolis; and speaker, House of Delegates, Dr. Haddon M. Carryer, Rochester. The president-elect, Dr. Clarence Jacobson, takes office immediately as president-elect. The other officers will take office on Jan. 1, 1960.

MISSOURI

Essay Contest on Medical History.—Establishment of the Arthur Rochford McComas Memorial Medical History Essay Contest was announced by the University of Missouri School of Medicine, Columbia. The contest, open to all students enrolled in the School of Medicine, will be based on essays on some subjects from Missouri medical history or from general medical history. It will offer an annual first prize of $100. The initial contest will be held during the 1959-1960 academic year, with essays to be submitted on or before April 1, 1960, to Mr. William K. Beatty, associate librarian at the Medical Center Library and associate professor of medical bibliography. Five faculty members from the School of Medicine and the university department of history have been selected to judge the essays. Dr. Arthur Rochford McComas, whom the contest memorializes, died in 1956 after having practiced medicine in Sturgeon for more than 50 years. During that period he was active in the Missouri State Medical

Association and served on the judicial council of the association for many years. He was association president in 1922-1923.

NEBRASKA

Dr. Egan Named Dean.—Dr. Richard L. Egan was appointed dean of the Creighton University School of Medicine, Omaha, to succeed Dr. Frederick G. Gillick, who resigned effective June 30 to become director of medical institutions for the County of Santa Clara, Calif. Dr. Egan joined the School of Medicine faculty in 1941 as an instructor and has been assistant dean since 1954. Currently serving as first vice-president of the Nebraska Heart Association, Dr. Egan was the organization's secretary last year. He is chairman of the Health Council of United Community Services in Omaha and is serving on the executive board of the Omaha-Douglas County Medical Society.

NEW YORK

Opening of Narcotic Unit.—The first patients will soon be admitted to the state's research unit in narcotic addiction, Dr. Paul H. Hoch, Commissioner of Mental Hygiene, revealed. There will be 55 beds for inpatients at the research center. In addition, about 150 outpatients will be treated. In the course of a year several hundred patients can be treated. The unit, located at Manhattan State Hospital, Wards Island, New York City, is the first full-time narcotics research unit in the state combining laboratory, outpatient, and inpatient operations. It has been organized for research purposes and will concentrate on basic investigations in an effort to determine primarily the causes of narcotic addiction and to develop better treatment methods. The work of the center will be integrated with the new program of treatment and clinical research to be conducted by the City of New York. At the present time, personnel are being recruited and trained for the unit, Dr. Hoch said. Three hospital staff members (a supervising nurse and two head nurses) are participating in a two-months' training course at the U. S. Public Health Service Hospital at Lexington, Ky., and will carry out a training program at the Manhattan research unit on their return. The staff will include psychiatrists, nurses, psychologists, social workers, laboratory research scientists (biochemists and physiologists), occupational and recreational personnel, and attendants.

Graduate Training.—Albany Medical College of Union University is accepting applications for admission to its graduate training program. The course of study leads to a Ph.D. degree in the basic medical sciences. Applicants must have a bachelor's degree, with a certain minimum of credits in science subjects. Studies begin in September, or earlier if the applicant wishes. Fellowships are generally available. These grants-in-aid defray almost all costs, including tuition and formal fees, as well as a large share of living expenses. Graduates of the program are qualified for a career as a teacher in the basic medical sciences, or as a medical or industrial research scientist. The Ph.D. degree, awarded by Union University, is available in the following specialties: anatomy, biochemistry, pathology, pharmacology, and physiology. Studies are usually completed in a four-year period. The curriculum covers three areas: (a) basic biomedical subjects, such as biochemistry, physiology, and anatomy; (b) special courses offered by each of the departments concerned; (c) research in the department of choice. Optional courses can be arranged at Rensselaer Polytechnic Institute and Union College. The facilities of the State Health Department Laboratories and the Albany Medical Center are made available to students requiring them. Information and application forms can be obtained by writing to the Registrar's Office, or to the Chairman of the Graduate Study Committee, Albany Medical College, Albany 8, N. Y.

New York City

Dr. Buckstein to Lecture in Israel.—Dr. Jacob Buckstein, consultant in gastroenterology, Trafalgar Hospital, accepted the invitation of the dean of the medical faculty of the Hebrew University-Hadassah Medical School, Jerusalem, Dr. Moshe Rachmilewitz, to deliver a lecture to the staff and general medical public of that city. The subject of his lecture will be "The Small Intestine—Normal and Abnormal: A Clinical and Roentgenological Study." Dr. Rachmilewitz and Dr. Kalman J. Mann, director general of the Hadassah Medical Organization, are arranging for Dr. Buckstein's reception there in October.

Dr. Snow Awarded Medallion.—The 12th Alumni Medallion for Distinguished Service to American Medicine of the State University of New York Downstate Medical Center in Brooklyn was awarded during commencement exercises June 10 to Dr. William B. Snow. The physician received a bronze medal cast in a likeness of Aesculapius and a hand-lettered scroll from Dr. Robert A. Moore, president of the Medical Center, who cited him as "a distinguished alumnus and physician; healer of the sick; mender of the disabled; pioneer, teacher and investigator in the specialty of physical medicine and rehabilitation."

Personal.—Dr. Lester J. Evans, executive associate of the Commonwealth Fund, accepted the post of director of New York University's Center for Rehabilitation Services, effective Nov. 1. Dr. Evans has been a member of the Commonwealth Fund's staff for 31 years. The fund is a philanthropic organization that supports activities intended to improve the health of the American people.—The Long

Island Consultation Center announced the appointment of Dr. Ludwig Fink as medical director. Dr. Fink formerly worked in the rehabilitation of alcoholics in Syracuse.—Dr. William J. Pyles became the new medical director of the New York Heart Association June 1, succeeding Dr. Daniel F. Milam, who retired.

Warning Labels for Plastic Bags.—Dr. Leona Baumgartner, commissioner of health, announced June 15 that the Board of Health has taken action to protect users of plastic bags against suffocation by adopting an amendment to the Sanitary Code which requires that a warning label be placed on every plastic bag under 1 mil in thickness and the length and width of which adds up to 25 in. or more. The required warning is as follows:

> WARNING—TO AVOID DANGER OF SUFFOCATION KEEP AWAY FROM BABIES AND CHILDREN. DO NOT USE IN CRIBS, BEDS, CARRIAGES OR PLAY PENS. THIS BAG IS NOT A TOY.

Under this amendment to the Sanitary Code, persons in New York City who "sell or hold for sale at retail or give away" such plastic bags are required to affix a label or tag to the bag or have imprinted on the plastic in conspicuous letters this warning label.

Former Residents Honor Dr. Browder.—Twenty-three of 25 former residents who completed their training in neurosurgery at the Kings County Hospital in Brooklyn since 1934 returned on June 12 to pay tribute to their former chief, Dr. E. Jefferson Browder, head of neurosurgery at the hospital and professor of neurosurgery at the State University of New York Downstate Medical Center across the street. Highlight of the day's program was the presentation to Dr. Browder of a leatherbound book entitled "To The Boss," consisting of a handwritten memoir of his experiences under Dr. Browder from each of the former residents. A scientific session held at the Kings County Hospital in the afternoon included eight papers describing recent experimental work being carried out by the former residents. Dr. H. Russell Meyers, one of the former residents and now chairman of the department of neurosurgery at the University of Iowa, delivered the after-dinner speech, "Neurosurgery: Current Trends and the Future Development."

OHIO

Visiting Professors on Hospital Program.—The Youngstown Hospital Association has listed the following guest speakers in connection with its visiting professorship program for the remainder of 1959: Dr. James A. Curtin, University of Buffalo; Dr. Lawrence E. Young, University of Rochester; Dr. Oliver S. Moore, Cornell University; and Dr. Simon Rodbard, University of Buffalo.

Dedicate Radiation Laboratory.—Paul C. Aebersold, Ph.D., director, Atomic Energy Commission's Office of Isotopes Development, was the guest speaker at the dedication of the Picker Research Center, Cleveland. The one-million-dollar center, a commercial radiation laboratory built by Picker X-Ray Corporation, will process and package radioisotopes for medical and industrial users throughout the world. The center will also do research on the processing and packaging of isotopes. The radioisotope laboratory is equipped for quick processing and packaging of "almost any radioisotope in quantities up to a million curies of cobalt 60 or its equivalent." Storage facilities for some 100,000 curies of isotopes are provided in 54 vertical storage tubes. Encapsulation of isotopes or experiments in the test cell can be observed through a special window more than five feet thick, filled with a zinc-bromide solution. The rear of the test cell is closed by a door five feet thick that weights about 40 tons. The 100,000-curie storage vault will also be used as a "gamma garden" in which scientists will be able to study the effects of gamma radiation on any material in samples up to a 17-inch cube in size. A radiochemical area, adjacent to the test cell and storage garden, will be used for work with low-intensity radiation sources. There will also be a "cold" (nonradioactive) chemical laboratory. The second floor of the center houses the instrument engineering section for research and development work on radiation detectors, electronics, and precision mechanical devices.

RHODE ISLAND

State Medical Election.—Dr. Alfred L. Potter, Providence obstetrician and gynecologist, was installed as the 100th president of the Rhode Island Medical Society, succeeding Dr. Francis B. Sargent. Other officers elected and installed were Dr. Earl J. Mara, Pawtucket internist, president-elect; Dr. Samuel Adelson, Newport, reelected vice-president; Dr. Arthur E. Hardy, Warwick, secretary; and Dr. James M. Beardsley, Providence, treasurer.

WISCONSIN

Course in Rehabilitation of Stutterers.—The first four-week course in the rehabilitation of the adult stutterer is offered at the University of Wisconsin, Madison, June 22-July 17 for practicing speech therapists who wish to increase their competence. Sponsored by the university in cooperation with the federal Office of Vocational Rehabilitation, the course enables the therapists to hear lectures and take part in group discussions with eight visiting specialists, each representing a specific point of view. Each visitor will give two lectures, interview a stutterer, and lead a group discussion. Therapy demonstrations by staff members of the university Speech and Hearing Clinics, made over closed-circuit TV, will be featured each day.

GENERAL

Film Library on Medical Technology.—A grant of $1,000 per year for three years to establish a film library was presented at the American Society of Medical Technologists' national headquarters in Houston, Texas. Mr. Paul A. Rohde, director of technical services, Baltimore Biological Laboratory, Inc., a division of Becton, Dickinson & Co., Baltimore, presented the grant to Elizabeth F. O'Connor, M.T. (ASCP), president, American Society of Medical Technologists. The fund will be used to purchase and distribute films and microslides for educational purposes among affiliated state and local groups of the society.

International Telephone Symposium.—On June 16 the first international telephone symposium on "The Effects of Estrogens in the Menopause" took place between physicians in the U. S. and Europe. The symposium was organized by the Excerpta Medica Foundation under a grant from Ayerst Laboratories. Three physicians in New York spoke for more than one hour with three European colleagues who were at the Royal Netherland Academy of Sciences in Amsterdam for the symposium. The moderator of the discussion was Dr. I. A. Wijsenbeek, an editor of "Excerpta Medica." Ayerst Laboratories plans to make the entire proceedings available for distribution to teaching institutions and individual physicians who are interested.

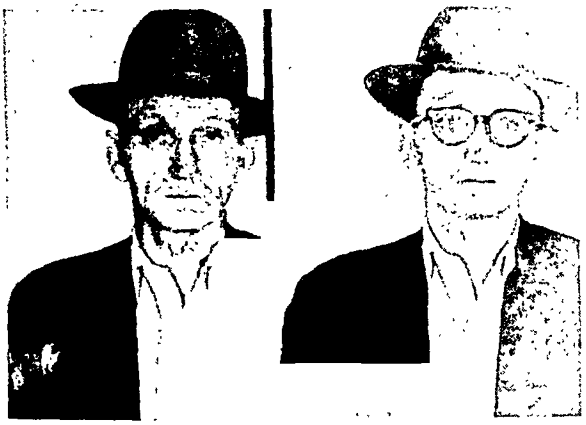
Accident Prevention.—The American Academy of Pediatrics has announced the availability of a bibliography on accident prevention prepared by the Committee on Accident Prevention of the academy. The bibliography was prepared for use of the academy's state committees on accident prevention, but the academy "would like to encourage its use wherever it might be an effective instrument." The contents of the bibliography are listed under 18 headings ranging from accident prevention as a world problem to teaching aids for medical students. A list of publishers and their addresses is also given. The academy will provide the bibliography without cost on request. For information, write the American Academy of Pediatrics, 1801 Hinman Ave., Evanston, Ill.

Scholarships for Neuromuscular Studies.—The Sister Elizabeth Kenny Foundation announced continuation of its program of postdoctoral scholarships to promote work in neuromuscular diseases. These scholarships are designed for scientists at or near the end of their fellowship training in either basic or clinical fields concerned with the broad problem of the neuromuscular diseases. The Kenny Foundation Scholars will be appointed annually. Each grant will provide a stipend for a five-year period at the rate of $5,000 to $7,000 a year, depending upon the scholar's qualifications. Candidates from medical schools in the United States and Canada are eligible. Inquiries regarding the program should be addressed to: Dr. Edgar J. Huenekens, Medical Director, Sister Elizabeth Kenny Foundation, Inc., 2400 Foshay Tower, Minneapolis 2, Minn.

Allergy Scholarships.—The Allergy Foundation of America announced the awarding of its $500 summer (or quarterly) scholarships for 1959 to 25 medical students from medical schools throughout the United States and Canada "so that these students might spend 8-12 weeks obtaining supervised training and experience in both clinical and research allergy." This is the largest number of these awards made by the foundation during any year since the scholarship program was begun in 1956. These awards are intended to encourage and assist medical students to obtain a broader knowledge and better understanding of the allergic diseases. The recipients participate actively in research in allergy or in the basic sciences related to allergy. These awards were made possible by grants to the Allergy Foundation of America by Mr. John D. Rockefeller Jr. and Mr. Robert J. Bauer. The students selected were nominated by the deans of their respective medical schools in collaboration with the heads of basic science departments at these institutions. The Allergy Foundation of America, 801 Second Ave., New York City, was established in 1953 to promote medical education and research in allergy and to provide the public with "authoritative information and advice."

Plan Large-Scale Cancer Study.—The American Cancer Society will launch a medical statistical study this fall to discover "why some people may be more likely to get cancer than others." The study will involve more than one million Americans. This is reportedly the first such large-scale family prospective study ever undertaken. The project, which will take six years to complete, will be conducted with the assistance of 50,000 trained American Cancer Society volunteers, it was announced by Dr. Eugene P. Pendergrass, American Cancer Society president. The study, under direction of Edward C. Hammond, Sc.D., American Cancer Society director of statistical research, also will probe the effect of environment on cancer and will attempt to learn more about symptoms of the disease to help improve early detection. Another major objective of the study is to find out what percentage of the public has undiagnosed cancer. A pilot study in five cities, Harrisburg, Pa.; Cleveland; Baltimore; Nashville, Tenn.; and Tampa, Fla., has already been conducted to test methods on more than 4,000 persons. In full swing, the project will attempt to study 500,000 families with more than one million persons who are at least 30 years of age. The 50,000 volunteer researchers will each select about 10 households which he or she can expect to trace for the following six years. Each family would be reported on annually. In addition to answering an original questionnaire, each subject will be required to fill out forms with supplementary information every two years.

Wanted by the F. B. I.—Edwin Sanford Garrison is one of the "ten most wanted fugitives" of the F. B. I. He may seek employment as an accountant, auditor, or bookkeeper. Following his escape on Aug. 23, 1958, from Kilby Prison, Montgomery, Ala., where he was serving a life sentence for robbery, Garrison became the subject of a federal complaint filed on Aug. 25, 1958, charging him with unlawful interstate flight to avoid confinement. Garrison has also been convicted for burglary, larceny, and murder. He should be considered dangerous. Garrison was born March 25, 1900, in Kentucky. He is 5 ft. 9½ in. tall, weighs 137 to 143 lbs., has a slender build, gray hair, blue eyes, and a medium complexion. He has two dim scars on the left side of the forehead, a scar on the right side of the forehead, a 1⅝ in. scar on the inner right eyebrow, scar on the right cheek, a ¼ in. scar on the right side of the upper lip, a scar on the back of the left hand, scars on the back of the right hand and wrist, a ½ in. scar on the left ring finger, a ¾ in. scar on the left index finger, burn scars on both lower legs, and a 2½ in. scar on the left biceps. Garrison wears false teeth and has been known to drink to excess. He has also been known as Arthur B. Beaumont, James Brown, George Coleman, James Gardner, Edwin Garretson, Edward Sanford Garrison, Gary Garrison, George E. Garrison, George E. Garry, George E. Martin, George F. Martin, George Walker, George E. Williams, George Walter Williams, "Brownie," and others. Persons having information concerning Garrison's whereabouts should call the nearest office of the F. B. I., whose telephone number is listed on the first page of any telephone directory.



Edwin Sanford Garrison.

Prevalence of Poliomyelitis.—According to the National Office of Vital Statistics, the following number of reported cases of poliomyelitis occurred in the United States, its territories and possessions in the weeks ended as indicated:

Area	June 13, 1959 Paralytic Type	June 13, 1959 Total Cases	June 14, 1958 Total
New England States			
Maine	..	..	..
New Hampshire	..	..	..
Vermont	..	..	..
Massachusetts	..	..	..
Rhode Island	..	..	..
Connecticut	..	..	..
Middle Atlantic States			
New York	..	..	1
New Jersey	..	..	1
Pennsylvania	..	..	..
East North Central States			
Ohio	1	2	..
Indiana	..	..	..
Illinois	..	..	..
Michigan	2	3	3
Wisconsin	..	..	..
West North Central States			
Minnesota	2	2	..
Iowa	9	11	1
Missouri	1	1	1
North Dakota	..	..	..
South Dakota	..	..	..
Nebraska	2	2	..
Kansas	2	3	..
South Atlantic States			
Delaware	..	..	1
Maryland	..	..	..
District of Columbia	..	..	..
Virginia	3	3	2
West Virginia	1	1	2
North Carolina	3	3	2
South Carolina	..	..	..
Georgia	2	2	2
Florida	2	3	13
East South Central States			
Kentucky	..	..	..
Tennessee	2	2	1
Alabama	2	2	..
Mississippi	1	1	3
West South Central States			
Arkansas	2	3	1
Louisiana	2	3	3
Oklahoma	5	6	1
Texas	2	5	10
Mountain States			
Montana	..	..	..
Idaho	..	..	..
Wyoming	..	..	..
Colorado	..	..	1
New Mexico	..	..	..
Arizona	1	2	..
Utah	..	..	..
Nevada	..	..	..
Pacific States			
Washington	..	..	..
Oregon	..	..	1
California	8	12	5
Alaska	..	..	..
Hawaii	..	..	3
Puerto Rico	..	..	..
Total	55	72	58

Grants to Aid Public Health Education.—The nation's 11 schools of public health have been awarded training grants totaling $450,000, the U. S. Public Health Service announced. Legislation authorizing such aid was passed in 1958 and funds were appropriated for it in the supplemental appropriation approved by President Eisenhower May 20. The funds will help the schools extend and improve specialty training in public health for physicians, nurses, engineers, and other personnel who are employed in federal, state, and local public health agencies in the United States and in foreign health agencies. The Public Health Service estimates that about 20,000 professional personnel employed in public health agencies in this country need additional training in modern methods for the investigation and control of disease and the maintenance of a healthful environment.

FOREIGN

Congress on Prophylactic Medicine in Austria.—The World Congress of Prophylactic Medicine and Social Hygiene will be held Aug. 29-Sept. 5 in Bad Aussee, Austria. The following program is arranged for the first scientific meeting:

Aug. 30—Main Theme: Foundations of Prophylactic Medicine.
Aug. 31—Main Theme: Prophylaxis of Allergic Diseases.
Sept. 1—Main Theme: Prophylaxis of Disturbances of the Heart and Circulation.
Sept. 2—Main Theme: Physical Medicine in Prophylactic View. For the second meeting on the same day: Campaign Against Rheumatism and Tuberculosis.
Sept. 3—Main Theme: Prophylactic Medicine and Geriatrics. For the second meeting on this day: General Problems of Prophylactic Medicine.
Sept. 4—Main Theme: Prophylaxis of Damage Caused by Civilization, and Mental Hygiene.

For information address the World Congress of Prophylactic Medicine and Social Hygiene, Bad Aussee, Salzkammergut, Austria.

CORRECTION

Niacin for Hypercholesteremia.—In the item bearing this title (June 6, page 714) under Denmark the fifth sentence should have read: "In all but one patient there was an appreciable fall of the serum cholesterol level during this treatment, and when it was discontinued it rose to the pretreatment level."

The Candidate for Coronary Heart Disease.—In the article by Gertler and associates (May 9 issue, page 149) an error was made in the preparation of the article for the printer. In the table "Results of Analysis" only the correlation coefficient $X_{1.9}$ should have a minus sign.

EXAMINATIONS AND LICENSURE

NATIONAL BOARD OF MEDICAL EXAMINERS

National Board of Medical Examiners: Various Centers: Part I only, Sept. 9-10. Examinations must be received at least six weeks in advance of a specific examination date. Examining centers established after close of registration. Exec. Sec., Dr. John P. Hubbard, 133 South 36th St., Philadelphia 4.

EDUCATIONAL COUNCIL FOR FOREIGN MEDICAL GRADUATES, INC.

Educational Council for Foreign Medical Graduates: Stations around the world, Sept. 22. Final date for filing applications was June 22. Succeeding examinations—March 16, 1960 and Sept. 21, 1960. Exec. Director, Dr. Dean F. Smiley, 1710 Orrington Ave., Evanston, Ill.

BOARDS OF MEDICAL EXAMINERS

Alaska:* On application in Anchorage or Fairbanks. Sec., Dr. W. M. Whitehead, 172 South Franklin St., Juneau.

Arizona:* *Reciprocity.* Phoenix, July 15-17. Exec. Sec., Mr. Robert Carpenter, 826 Security Bldg., Phoenix.

California: *Written.* Los Angeles, Aug. 17-20; Sacramento, October 19-22. *Oral.* Los Angeles, August 15; San Francisco, November 14. *Oral and Clinical.* Los Angeles, August 16; San Francisco, Nov. 15. Sec., Dr. Louis E. Jones, Room 536, 1020 N Street, Sacramento.

Colorado:* *Examination. Reciprocity.* Denver, July 14. Sec., Dr. John B. Farley, 712 Republic Bldg., Denver 2.

Connecticut:* *Examination.* Hartford, July 14-16. Sec., Dr. Staley B. Weld, 160 St. Ronan St., New Haven.

Delaware: *Examination.* Dover, July 14-16. *Endorsement.* Dover, July 23. Sec., Dr. Joseph S. McDaniel, Professional Bldg., Dover.

Guam: *Subject to Call.* Act. Sec., Dr. F. L. Conklin, Agana.

Hawaii: *Written.* Honolulu, July 13-14. Sec., Dr. I. L. Tilden, 1020 Kapiolani St., Honolulu.

Idaho: *Examination and Endorsement.* Boise, July 13. Exec. Sec., Mr. Armand L. Bird, 364 Sonna Bldg., Boise.

Maine: *Examination and Reciprocity.* Augusta, July 14-16. Sec., Dr. Stephen A. Cobb, Sanford.

Montana: *Examination and Reciprocity.* Helena, Oct. 6. Sec., Dr. Thomas L. Hawkins, 555 Fuller Ave., Helena.

New Hampshire: *Examination and Reciprocity.* Concord, Sept. 9-12. Sec., Dr. Edward W. Colby, 107 State House, Concord.

North Carolina: *Endorsement.* Blowing Rock, July 24. Sec., Dr. Joseph J. Combs, Professional Bldg., Raleigh.

Puerto Rico: *Examination.* San Juan, Sept. 8. Sec., Dr. Joaquin Mercado Cruz, Box 9156, Santurce.

South Dakota:* *Examination.* Sioux Falls, Aug. 25-26. Exec. Sec., Mr. John C. Foster, 300 First National Bank Bldg., Sioux Falls.

Washington:* *Examination.* Seattle, July 13-15. Administrator, Mr. Thomas A. Carter, Capitol Bldg., Olympia.

West Virginia: *Examination.* Charleston, July 13-15. *Reciprocity and Endorsement,* July 13. Sec., Dr. Newman H. Syer, State Office Bldg., No. 3, Charleston 5.

Wisconsin:* *Written.* Milwaukee, July 14-16. *Reciprocity.* Milwaukee, July 15. Sec., Dr. Thomas W. Tormey, Jr., 1140 State Office Bldg., Madison.

Wyoming: *Examination and Reciprocity.* Cheyenne, Oct. 5. Sec., Dr. James W. Shannon, State Office Bldg., Cheyenne.

BOARDS OF EXAMINERS IN THE BASIC SCIENCES

Alaska: *Examination and Reciprocity.* Juneau, November. Sec., Dr. R. Harrison Leer, Alaska Office Bldg., Juneau.

Iowa: *Examination.* Des Moines, July 14. Sec., Dr. Elmer W. Hertel, Waverly.

Oklahoma: *Examination.* Oklahoma City, Sept. 25-26. Exec. Sec., Mrs. L. Haidek, 813 Braniff Bldg., Oklahoma City.

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*Basic Science Certificate required.

DEATHS

Abel, Samuel E., Murfreesboro, Tenn.; University and Bellevue Hospital Medical College, New York City, 1931; specialist certified by the American Board of Psychiatry and Neurology; member of the American Psychiatric Association; veteran of World War II; on the faculty of Vanderbilt University School of Medicine in Nashville; director of professional services at the Veterans Administration Hospital; died in the Hamilton Hotel in Chicago April 22, aged 52.

Abrums, Horatio Ely Ⓜ Trinidad, Colo.; Georgetown University School of Medicine, Washington, D. C., 1903; veteran of the Spanish-American War; died in the Mount San Rafael Hospital April 13, aged 79.

Adams, Charles Clyde Ⓜ Atlanta, Ga.; Emory University School of Medicine, Atlanta, 1935; member of the American Academy of General Practice; veteran of World War I; died April 17, aged 58.

Alexander, Robert Berthold Ⓜ San Francisco; Schlesische-Friedrich-Wilhelms-Universität Medizinische Fakultät, Breslau, Prussia, 1925; member of the American Academy of General Practice; served in the German Army during World War I; a member of the San Francisco Selective Service Board during World War II; on the staffs of the Mount Zion, St. Mary's, Hahnemann, Franklin, and Notre Dame hospitals; died in the Mount Zion Hospital April 19, aged 65.

Bailey, Patrick Cleburn, Chicota, Texas; University of Nashville (Tenn.) Medical Department, 1907; died April 24, aged 81.

Baker, Karl Winter, Turtle Lake, Wis.; Wisconsin College of Physicians and Surgeons, Milwaukee, 1900; died in Luther Hospital, Eau Claire, April 9, aged 81.

Baker, John J., Cutshin, Ky.; Lincoln Memorial University Medical Department, Knoxville, Tenn., 1913; on the staff of the Mount Mary Hospital in Hazard; died April 8, aged 84.

Banfield, Samuel Richard Ⓜ Highland Park, Ill.; Rush Medical College, Chicago, 1928; on the staff of the Highland Park Hospital; died in the North Shore Hospital, Winnetka, April 25, aged 58.

Barry, Roy Joseph, Boston; born in Quincy, Mass., March 7, 1924; Tufts College Medical School, Boston, 1951; interned at Hartford (Conn.) Hospital, where he served a residency; served a residency at the Massachusetts General Hospital in Boston and the Oak Ridge Institute of Nuclear Studies, medical division, Oak Ridge, Tenn.; specialist certified by the American Board of Radiology; certified by the National Board of Medical Examiners; served in the Army for three years in World War II with assignments in the Philippines and in Japan; from April, 1953, to December, 1954, was a first lieutenant with the U. S. Air Force serving as a flight surgeon with a jet fighter group based at Chaumont, France; assistant in radiology at the Massachusetts General Hospital; died April 19, aged 35.

Bell, James Francis, Portland, Ore.; University of Oregon Medical School, Portland, 1917; served in the regular Navy; veteran of World War I; died in the Veterans Administration Hospital April 13, aged 68.

Belt, Francis Behring Ⓜ Hermiston, Ore.; State University of Iowa College of Medicine, Iowa City, 1921; charter president of the Hermiston Rotary Club; past-president of the Hermiston Chamber of Commerce; served on the staff of St. Anthony Hospital in Pendleton and the Good Shepherd Hospital, where he was first president of the staff, and where he died April 24, aged 62.

Bethell, Frank Hartsuff Ⓜ Ann Arbor, Mich.; born in New York City April 11, 1903; Johns Hopkins University School of Medicine, Baltimore, 1929; member of the Association of American Physicians, Central Society for Clinical Research, Michigan Academy of Science, American Society for Clinical Investigation, Arts and Letters, Phi Beta Kappa, Sigma Xi, and the American Society for Experimental Pathology; fellow of the American College of Physicians; past-president of the Washtenaw County Medical Society; professor of internal medicine since 1949 at the University of Michigan Medical School, where he joined the faculty in 1931 as instructor of internal medicine, subsequently becoming assistant professor and associate professor; in 1939 received the Henry Russel Award, the highest honor the university can bestow on an assistant professor, the rank he held at that time; from 1943 to 1950 medical director of the curriculum in medical technology in the College of Literature, Science and the Arts; in 1952 appointed to the radiation policy committee of the university and in 1958 to the dean's committee of the Veterans Administration Hospital; since September, 1956, director of the Simpson Memorial Institute, at the University of Michigan Medical School, where from 1931 to 1942 he was a research assistant,

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Ⓜ Indicates Member of the American Medical Association.

from 1942 to 1954 an assistant director, and associate director from 1954 to 1956; for five years principal investigator of the Atomic Energy Commission project on biological effects of irradiation; associated with the University Hospital; died April 21, aged 56.

Edwards, Howard Keay Ⓜ Miami, Fla.; born in London, England, May 10, 1910; Washington University School of Medicine, St. Louis, 1936; specialist certified by the American Board of Preventive Medicine; member of the American College of Chest Physicians, American Trudeau Society, and the Industrial Medical Association; joined the medical staff of Eastern Air Lines in May, 1941, and shortly thereafter was appointed the company's medical director, which post he held at the time of his death; associated with James M. Jackson Memorial Hospital; died at Lake Tahoe, Calif., April 18, aged 48, while en route to attend the annual meeting of the Aero Medical Association, of which he was a founder and for the past three years a member of its executive council.

Ehrmann, Calder De Bruler Ⓜ Rockport, Ind.; Chicago Homeopathic Medical College, 1900; veteran of World War I; died in Webster Groves, Mo., March 21, aged 80.

Elmore, Ralph De Witt, Denver, Colo.; Kansas Medical College, Medical Department of Washburn College, Topeka, 1899; served as director of the National Farmers Union Insurance Company; died April 4, aged 83.

Fender, Asa Harrel Ⓜ Worthington, Ind.; Indiana University School of Medicine, Indianapolis, 1937; veteran of World War II; died in St. Vincent's Hospital, Indianapolis, April 11, aged 46.

Fiset, Louis Oliver Ⓜ Seattle; University of Toronto Faculty of Medicine, Toronto, Ont., Canada, 1894; died in the Swedish Hospital April 10, aged 89.

Fritschi, Ulrich Alfred Ⓜ Sacramento, Calif.; University of California School of Medicine, San Francisco, 1941; specialist certified by the American Board of Ophthalmology; member of the American Academy of Ophthalmology and Otolaryngology and the Association for Research in Ophthalmology; served on the faculty of his alma mater; veteran of World War II; senior staff member at Sutter General Hospital, where he died April 5, aged 51.

Garside, Francis Vincent Ⓜ Providence, R. I.; Harvard Medical School, Boston, 1922; member of the International College of Surgeons; treasurer of the Rhode Island Medical Society; secretary of the state board of medical examiners; member and past-president of the staff of Our Lady of Fatima Hospital; associated with St. Joseph's, Rhode Island, Charles V. Chapin, and Roger Williams General hospitals; died in Our Lady of Fatima Hospital April 7, aged 62.

Heironimus, Tarring Whitfield Jr. Ⓜ Grafton, W. Va.; University of Virginia Department of Medicine, Charlottesville, 1929; past-president of the Taylor County Medical Society; on the staff of the Grafton City Hospital; died April 5, aged 56.

Hensel, Charles Norton Ⓜ St. Paul; University of Minnesota College of Medicine and Surgery, Minneapolis, 1908; specialist certified by the American Board of Internal Medicine; fellow of the American College of Physicians; past-president of the Minnesota Heart Association and the Minnesota Academy of Medicine; served on the staffs of the St. Luke's Hospital and the Miller Hospital, where he died April 6, aged 77.

Hindman, Samuel Ⓜ Columbus, Ohio; Starling-Ohio Medical College, Columbus, 1910; veteran of World War I; served on the staffs of the Veterans Administration in Cleveland and Columbus; died *in the Veterans Administration Hospital in Dayton,* April 6, aged 79.

Jacoby, Adolph Ⓜ New York City; born in 1888; Cornell University Medical College, New York City, 1909; served as supervising physician of the city health department's syphilis and gonorrhea clinics from 1916 to 1935, when he was named medical supervisor of the newly created bureau of social hygiene, becoming director in 1950, retiring in 1952, after 36 years of service; special consultant to the U. S. Public Health Service and clinic consultant to the New York State Department of Health; served on the faculty of Post-Graduate Medical School of the New York University–Bellevue Medical Center; specialist certified by the American Board of Obstetrics and Gynecology; fellow of the American College of Surgeons; served on the staff of the Beth Israel Hospital; died April 12, aged 71.

Jaenichen, Robert Fritz Tobias Ⓜ Saginaw, Mich.; Detroit College of Medicine and Surgery, 1922; on the staff of St. Luke's Hospital; died March 31, aged 61.

Jaquith, Walter Allen, Columbus, Ohio; Queen's University Faculty of Medicine, Kingston, Ont., Canada, 1898; served as medical director of the Prudential Insurance Company in Newark, N. J.; retired medical director of the Columbus Mutual Insurance Company; past-president of the Association of Life Insurance Medical Directors of America; died in St. Anthony Hospital April 2, aged 84.

Jones, Stephen George Ⓜ Arlington, Mass.; Harvard Medical School, Boston, 1921; specialist certified by the American Board of Surgery; fellow of the American College of Surgeons; associated with the Symmes Arlington Hospital; served on the staffs of the Chelsea (Mass.) Memorial Hospital, Union Hospital in Lynn, Revere (Mass.) Memorial Hospital, and the Massachusetts General Hospital in Boston; died in the Phillips House of the Massachusetts General Hospital, Boston, April 9, aged 65.

Kinley, John William Ⓜ Summit, N. J.; McGill University Faculty of Medicine, Montreal, Que., Canada, 1931; specialist certified by the American Board of Psychiatry and Neurology; fellow of the American Psychiatric Association; served on the staffs of the St. Barnabas Medical Center in Newark and the Overlook Hospital; died April 12, aged 56.

Koravko, Mstislav Klement Ⓜ San Francisco; University of Moscow Faculty of Medicine, Russia, 1919; associated with French Hospital; died April 13, aged 70.

Kurtin, Joseph James Ⓜ Cudahy, Wis.; born in Cudahy May 2, 1926; Marquette University School of Medicine, Milwaukee, 1949; specialist certified by the American Board of Pathology; assistant professor of pathology at his alma mater; interned at St. Joseph's Hospital in St. Paul; served a residency at St. Mary's Hospital in Milwaukee and the Veterans Administration Center in Wood; for two years a medical officer in the medical corps of the U. S. Army Reserve; director of the department of pathology at Trinity Memorial Hospital; assistant pathologist at St. Francis Hospital in Milwaukee; died in the Veteran Administration Hospital, Wood, April 12, aged 32.

Leikensohn, Abraham Ⓜ Staten Island, N. Y.; Université de Geneve Faculté de Médecine, Switzerland, 1936; president-elect of the Richmond County Medical Society, of which he was for many years treasurer; on the staff of St. Vincent's Hospital; died April 13, aged 50.

Loewenstein, Ludwig Wilhelm Ⓜ New York City; Universität Köln (Cologne) Medizinische Fakultät, Köln, Prussia, 1922; specialist certified by the American Board of Dermatology and Syphilology; member of the American Academy of Dermatology and Syphilology; on the staff of the New York Skin and Cancer Hospital unit of University Hospital–Bellevue Medical Center; died April 15, aged 63.

Long, J. Bradley Ⓜ San Francisco; born in Portsmouth, N. H., Nov. 24, 1922; New York University College of Medicine, 1946; specialist certified by the American Board of Internal Medicine; interned at the Mary Hitchcock Memorial Hospital in Hanover, N. H.; served a residency at the Peter Brigham Hospital in Boston and Stanford University Hospitals in San Francisco; assistant clinical professor of medicine, University of California School of Medicine, where he was assistant director of the cardiac clinic; since 1952 clinical instructor in medicine at Stanford University School of Medicine; vice-president of the San Francisco Heart Association; served in the medical corps of the U. S. Naval Reserve from 1947 to 1949; staff member at Children's Hospital, St. Mary's, Stanford University, and Notre Dame hospitals, and the University of California Hospitals; died April 9, aged 36.

McCalib, David Crockett Ⓜ Colbert, Okla.; Barnes Medical College, St. Louis, 1909; served on the staff of Durant (Okla.) Hospital; died April 1, aged 73.

McCandless, Harvey Galt Ⓜ Cincinnati; University of Cincinnati College of Medicine, 1933; interned at the University Hospitals in Iowa City; served a residency at the Cincinnati General Hospital; member of the American Urological Association; fellow of the American College of Surgeons; veteran of World War II; at one time secretary of the Cincinnati Academy of Medicine; served on the staffs of the Christ and Children's hospitals; died April 5, aged 51.

McGroarty, John James Ⓜ Easton, Minn.; University of Minnesota College of Medicine and Surgery, Minneapolis, 1907; past-president of the Blue Earth Valley Medical Society; in 1957 was honored at Sioux Falls, S. D., as the "Catholic rural doctor of the year"; served as health officer; died in the Wells (Minn.) Hospital April 6, aged 78.

Magill, Samuel Rufus Ⓜ Springfield, Ill.; Bennett Medical College, Chicago, 1913; served in France during World War I; on the staffs of St. John's Hospital and the Memorial Hospital, where he died April 4, aged 68.

Martin, William Bo Ⓜ La Porte, Ind.; University of Michigan Medical School, Ann Arbor, 1933; past-president of the La Porte County Medical Society; associated with Holy Family and Fairview hospitals; died April 5, aged 51.

Mason, Everett Lee Ⓜ Eau Claire, Wis.; Chicago Homeopathic Medical College, 1903; Northwestern University Medical School, Chicago, 1909; veteran of World War I; medical director of the National Mutual Benefit Life Insurance Company of Madison; on the staffs of the Luther Hospital and the Sacred Heart Hospital, where he died April 5, aged 80.

Moody, Rollen Wayne Ⓜ Denver; University of Colorado School of Medicine, Denver, 1940; interned at the Denver General Hospital, where he served a residency; served a residency at the Colorado General Hospital; certified by the National Board of Medical Examiners; specialist certified by the American Board of Internal Medicine; fellow of the American College of Physicians; associate clinical professor of medicine at his alma mater; associated with Denver General, Colorado General, Mercy, General Rose Memorial, and St. Anthony hospitals; died April 5, aged 44.

Moulton, William A. Ⓜ Candor, N. Y.; New York University Medical College, New York City, 1897; served as health officer of the town of Candor and coroner for Tioga County for many years; associated with the Tompkins County Memorial Hospital, Ithaca, and the Tioga County General Hospital in Waverly, where he died April 5, aged 87.

Murdoch, Franklin Forman Ⓜ Captain, U. S. Navy, retired, Bremerton, Wash.; New York Homeopathic Medical College and Hospital, New York City, 1911; specialist certified by the American Board of Internal Medicine; fellow of the American College of Physicians; entered the U. S. Navy in 1917; retired in 1947; veteran of World Wars I and II; at one time executive officer of the U. S. Naval Hospital; in 1931 appointed professor of tropical medicine at George Washington University School of Medicine in Washington, D. C.; head of the clinic at Washington Veterans Home, Retsil; died April 3, aged 69.

Nathanson, Elias S., Lynn, Mass.; University of Maryland School of Medicine, Baltimore, 1908; served on the staffs of the Union Hospital and the Lynn Hospital, where he died April 6, aged 75.

Osborne, Norman Bellinger, Andover, Ohio; Hahnemann Medical College and Hospital of Philadelphia, 1908; veteran of World War I; died April 2, aged 74.

Parkison, Wallace Moore, Long Beach, Calif.; Medical College of Indiana, Indianapolis, 1904; on the selective service board during World War II; died April 5, aged 81.

Pence, Winfield Scott Ⓜ San Saba, Texas; University of Texas School of Medicine, Galveston, 1928; member of the school board; veteran of World War I; past-president of the Rotary Club; served on the staff of the San Saba Memorial Hospital, where he died April 9, aged 68.

Potter, Alfred Hollister, Springfield, Ohio; Starling-Ohio Medical College, Columbus, 1909; fellow of the American College of Surgeons; veteran of World War I; associated with the City Hospital, where he was a member of the board of trustees and past-president of the medical staff; on the staff of the Mercy Hospital; for many years surgeon for the New York Central Railroad; died April 4, aged 77.

Rabenneck, Paul Benjamin Ⓜ Nashville, Ill.; St. Louis University School of Medicine, 1912; past-president of the Southern Illinois Medical Association and the Washington County Medical Society; served as county coroner; veteran of World War I; died in the Missouri Pacific Hospital in St. Louis April 9, aged 72.

Reardon, John Stephen, New Rochelle, N. Y.; University of Michigan Department of Medicine and Surgery, Ann Arbor, 1912; past-president of the New Rochelle Medical Society; veteran of World War I; deputy health officer of New Rochelle; for 31 years school physician in parochial schools; on the staff of the New Rochelle Hospital, where he died April 10, aged 70.

Reid, Robert Scott, Oceanside, Calif.; Starling Medical College, Columbus, 1898; died March 24, aged 82.

Richards, Daniel Fred Ⓜ Denver; Denver and Gross College of Medicine, 1905; died March 9, aged 77.

Robb, John Oswald Ⓜ Hillsboro, Ore.; University of Toronto Faculty of Medicine, Toronto, Ont., Canada, 1907; served on the school board and city council; president of the Washington Federal Savings and Loan Association; on the staff of the Quality Community Hospital; died April 4, aged 78.

Shade, Virgil Edward, Inglewood, Calif.; St. Louis University School of Medicine, 1919; for many years practiced in St. Louis; died in the Veterans Administration Hospital, Los Angeles, April 3, aged 67.

Roney, Eugene Henry Ⓜ Detroit; Wayne University College of Medicine, Detroit, 1934; veteran of World War II, was decorated with the Purple Heart and was awarded the Bronze Star with two Oak Leaf Clusters; fellow of the American College of Obstetricians and Gynecologists; associated with the Mount Carmel Mercy Hospital, where he died April 10, aged 51.

Rosenbluth, Michael, New York City; Columbia University College of Physicians and Surgeons, New York City, 1902; specialist certified by the American Board of Otolaryngology; member of the American Academy of Ophthalmology and Otolaryngology; on the staffs of the Harlem and Lebanon hospitals; died March 19, aged 77.

Sargent, Arthur Forrest, Boston; Harvard Medical School, Boston, 1915; visiting orthopedic surgeon to the Pittsfield (Mass.) General Hospital, and the Cambridge City Hospital, where he died March 24, aged 71.

Skloff, Samuel Harry Ⓜ Philadelphia; Jefferson Medical College of Philadelphia, 1938; also a graduate in pharmacy; specialist certified by the American Board of Ophthalmology; interned at Mount Sinai Hospital in Philadelphia; served a residency at the Episcopal Eye, Ear and Throat Hospital in Washington, D. C.; on the staffs of the Northeastern and Episcopal hospitals; died April 16, aged 53.

Spackman, James Guie Ⓜ Wilmington, Del.; Hahnemann Medical College and Hospital of Philadelphia, 1912; served on the faculty of his alma mater; member of the founders group of the American Board of Surgery; fellow of the American College of Surgeons; served overseas during World War I; consulting surgeon at the Memorial Hospital; died April 9, aged 69.

FOREIGN LETTERS

CHILE

Shortage of Physicians and Nurses.—Dr. Valenzuela, executive director of the National Health Service (NHS), stated that a shortage of physicians and nurses is delaying the improvement of the level of public health in Chile. The 5,500,000 persons enrolled in the NHS must be cared for by only 2,200 physicians and less than 2,000 nurses. The NHS needs 700 new physicians to occupy vacancies chiefly in rural areas. The total population is 7,000,000. About 1,500,000 persons and 1,800 physicians remain outside the NHS. Pediatricians and obstetricians are especially needed. Vacancies in these two categories in January and February were filled by medical students undergoing special training. Chile's three medical schools graduate only about 180 physicians per year. The shortage of nurses is even more acute. About 400 nurses educated in Chile are now working in the United States and the Caribbean area because the rate of pay is so low in their own country, about 50 dollars (U. S. equivalent) per month.

Diastolic Pressure.—R. Cruz-Coke (*Rev. med. Chile* 87:116, 1959) studied the rate of rise of arterial pressure in relation to age in a group of 250 apparently healthy men registered with the national service of preventive medicine in Santiago. These subjects were selected because their blood pressure had been observed for more than 10 years. In the first examination all the subjects had diastolic blood pressures under 110 mm. Hg. The 250 subjects were followed up for an average period of 12 years. They were separated into five-year age groups at the first examination. In all groups the mean diastolic pressure increased with age, from 71.8 mm. Hg in the 20-to-24-year group to 90.7 mm. Hg in the 60-to-64-year group. In the last examination of each group 19 subjects had a diastolic pressure of over 110 mm. Hg.

In the total series the rate of rise of diastolic pressure was 0.35 mm. Hg per year from 22.5 to 42.5 years of age, and of 0.61 mm. Hg per year from 42.5 to 62.5 years of age. In the nonhypertensive group of 231 subjects the rate of rise was 0.31 mm. Hg per year from 22.5 to 52.5 years of age, and 1.06 mm. Hg per year from 52.5 to 62.5 years of age. The group of 19 apparently hypertensive subjects had a rate of rise of 1.14 mm. Hg per year from a mean age of 39.7 to 48.2 years of age, and of 8.64 mm. Hg per year from a mean age of 48.2 to 51.8 years of age. The author concluded that the rate of rise of the diastolic pressure in relation to age was an essential component of the quantitative study of blood pressure and was fully as important as the height of the pressure.

DENMARK

Phenylbutazone.—A series of 180 patients suffering from various diseases of the joints was treated with phenylbutazone by E. Jesting and co-workers (*Ugeskrift for laeger*, Feb. 19, 1959). The drug was given in tablet form, 800 mg. on the first day and 200 mg. daily on the succeeding days. It was discontinued if at the end of the first week there was no definite improvement. The patients still taking the drug at the follow-up examination underwent hematological studies. Of the 71 patients suffering from osteoarthritis deformans 24 had a satisfactory response, and 12 of these were still taking the drug. Of the 52 patients suffering from rheumatoid arthritis 10 had a satisfactory response. The best results were those obtained in patients with gout, all nine of these reacting in a few hours with diminution of pain, swelling, and fever. Those who had recurrences of gout responded well to further treatment with the drug. Side-effects, such as itching, rash, dryness of mouth and throat, epigastric distress, nausea, diarrhea, giddiness, and headache were observed in 27 patients, but, except for melena in 2 and neutropenia in one, the side-effects were not severe and no patient developed agranulocytosis. The authors concluded that if a patient failed to respond to a maintenance dose of 200 mg. the dose should be increased to 400 mg. daily before abandoning therapy. Phenylbutazone should be used only in patients who suffer from severe joint disease and in whom a definite response is obtained.

Poisoning in Children.—O. Aagenaes (*Ugeskrift for laeger*, Feb. 19, 1959) studied a series of 94 deaths, from 1941 to 1955, from poisoning (carbon dioxide poisoning not included) among children under the age of 5 years. Under the age of 1 year the sex incidence was the same, but between the ages of 1 and 5 years twice as many boys died from poisons as girls. Deaths from barbiturates numbered 12 in the first five years covered by the study, 13 in the second, and only 2 in the third, a fall reflecting the improved treatment given such patients in the third period. A similar fall was observed with regard to adults poisoned by barbiturates.

The items in these letters are contributed by regular correspondents in the various foreign countries.

Pernicious Anemia Among Neighbors.—N. J. Thomsen (*Ugeskrift for laeger,* March 5, 1959) cited E. Mogensen's report in 1952 which drew attention to the behavior of pernicious anemia in the town of Herning. In the course of about four months 12 new cases occurred in this town, whereas the average had previously been only 1, 2, or at the most 4 such cases yearly. Thomsen investigated the 98 patients treated at the Herning hospital between 1939 and the fall of 1956. By questioning 47 physicians practicing in the neighborhood he obtained data about 21 other patients, and by adding 6 collected by other means he brought his total to 125. After the deduction of the 10 who died there remained 115 patients who could be questioned about where they had lived from time to time, the occurrence of the disease in other members of the family, and other pertinent data. Thirty-four patients could tell of the occurrence of the disease in neighbors, friends, or acquaintances not their blood relatives. Speculating on the possibility that of these some at least were caused by a deficiency of some important factor in the environment, Thomsen drew attention to what may be a parallel state of affairs in cattle, due probably to a lack of cobalt in the soil.

Nitrofurantoin for Urinary Infections.—Jespersen and Askrog (*Ugeskrift for laeger,* March 5, 1959) used nitrofurantoin to treat an unselected series of 100 patients (72 men and 28 women) whose ages ranged from 16 to 88 years. The dosage was 100 mg. four times daily for six days. In many patients the infection had proved refractory to sulfonamides or antibiotics. In 21 the urine was sterile when the nitrofurantoin was discontinued, and in 41 others pyuria was much reduced or the symptoms were appreciably diminished. Of the 15 showing side-effects 13 were nauseated. This was avoided by administering tablets so coated as to delay the action of gastric juice on them. Hence the author concluded that the nausea was due to irritation of the gastric mucosa and not to any emetic action provoked by the drug after absorption.

GERMANY

Sex Incidence of Disease.—H. Franke and co-workers (*Deutsche med. Wchnschr.* 84:653, 1959) studied a series of 9,437 outpatients in the polyclinic of Würzburg University medical school. Predominant conditions in men were coronary disease; pulmonary diseases, including bronchial asthma; gastrointestinal disorders, including hyperacidity; chronic hepatic diseases; and all forms of tuberculosis. Those most frequently found in women were arteriosclerotic degeneration of the myocardium, goiter, hyperthyroidism, hepatic disease, essential hypochromic anemia, and autonomic imbalance. The authors believed that physiological differences between men and women were partially responsible for differences in sex incidence of internal diseases. A difference in the extent of exposure to certain stresses may also play a role in the variation in sex incidence.

Erythrocytes in Polycythemia.—K. Richter and G. Brüschke (*Med. Klin.* 54:16, 1959) stated that various opinions concerning the pathogenesis of polycythemia vera have been held since the disease was first described. Most investigators now regard the disease as neoplastic, with increased erythropoiesis, abnormal rise of total erythrocytes, and increased decomposition of erythrocytes. The quantitative relation among these three factors is essentially influenced by the life span of the red blood cells. Huff and co-workers in their studies with radioactive iron showed the diurnal plasma iron turnover in polycythemia vera to surpass by far the extent required for hemoglobin synthesis. This finding suggested that the longevity of these erythrocytes was shortened. London and co-workers who investigated the longevity of erythrocytes in polycythemia vera with the use of radioactive nitrogen-tagged glycine, reported, on the other hand, a rapid increase of specific activity of the hemoglobin in the first 5 days after using the glycine, followed by a decline and a second increase of activity between the 40th and 50th days. They concluded that two types of erythrocytes were present, one with an abnormally short and one with a normal life span.

To determine whether similar results could be obtained with the use of a different type of labeling of red blood cells Richter and Brüschke observed the life span of erythrocytes in 12 patients with polycythemia vera by tagging them with radioactive chromium (Cr^{51}). Eight of the patients previously had been treated with radioactive phosphorus (P^{32}), and two had been treated with x-rays. The last dose of P^{32} had been given 4 to 24 months earlier. None of the patients received a hemolytic agent. A chromium uptake by the blood cells of about 50% in three to five minutes was observed. Blood samples for evaluating the decline of activity were taken after 24 hours and then at intervals of one to three days after tagging. The time in which the initial activity declined to 50%, the half-life of the isotope, was considered the life time of erythrocytes. It averaged 31 days in healthy subjects. Proceeding from the mean half-life of Cr^{51} and taking the normal erythrocyte life span as 120 days, the mean erythrocyte life span in polycythemia vera was about 89 days. This life span was markedly reduced in eight patients and in four it was within the normal range. No relation between the severity and duration of the disease and type of pretreatment, on the one hand, and the life span of erythrocytes, on the other, was observed. The activity curves gave no indication of the concurrence of two erythrocyte populations with different life spans.

INDIA

Acetazolamide for Glaucoma.—Dhurandhar and Albal (*Journal of Postgraduate Medicine*, vol. 5, January, 1959) treated 50 patients who had glaucoma with acetazolamide. Another group of 18 such patients who received other drugs served as controls. The patients were classified according to the symptoms and tension as acute congestive, chronic congestive, chronic simple, and secondary glaucomas. In all acute cases except one the angle of the anterior chamber was blocked either by anterior synechias or by pigment in the trabeculas, as revealed by gonioscopy. Two patients with chronic congestive glaucoma also showed pigment in the trabeculas. The gonioscopic findings did not change after successful treatment with acetazolamide. The presence or absence of iridocyclitis could be determined by the use of slit-lamp microscopy. Results after therapy were assessed mainly by changes in the tension of the eyeball. Other criteria were improvement in vision, subjective improvement, and clearing of corneal edema in acute cases. Patients with moderately severe cases were given 250 mg. of the drug every eight hours, and those with acute cases received 250 mg. intravenously twice daily. No diuresis or serious side-effects were met with when this dosage schedule was used.

In most of the patients therapy with acetazolamide was followed by operation to prevent repeated attacks of glaucoma, in spite of encouraging results with the drug, because most of the patients attending free hospitals were likely to stop taking the drug after obtaining temporary relief. Only two patients with chronic glaucoma received acetazolamide for a period of four months. The drug was found to be useful in all varieties of glaucoma. All but 4 of the 50 patients showed a moderate or good response. The control group was treated with miotics, injections of 50% dextrose, or both, and there were more failures than successes with this treatment (only two showed a good response). Operation had to be offered to these patients as a compulsory measure. In two patients with acute glaucoma in whom miotics had failed to control the tension acetazolamide brought about a dramatic reduction in tension. Of 17 patients with acute glaucoma 9 were treated with the drug and 8 with a combination of acetazolamide and miotics. These latter showed signs of relief earlier than the former in whom acetazolamide alone was used. Subjective relief was felt on the first day with disappearance of corneal edema and reduction in congestion, while the tension came down gradually within a day or two.

In secondary glaucomas acetazolamide helped to reduce the tension and thus allowed the use of mydriatics. The drug was used preoperatively in nine patients who had glaucoma associated with cataract, five of whom showed good response. This made it possible to remove the cataract on the third day of treatment. The incidence of postoperative complications was reduced by controlling the tension before operation. As the therapy was not prolonged in any of the cases, no serious side-effects were noted. Some patients complained of dyspepsia, paresthesia, and numbness in the fingers and toes but these did not require discontinuing the drug.

Excretion of Niacin in Women.—Chitre and Bhatia (*Journal of Postgraduate Medicine*, vol. 5, January, 1959) studied the excretion of niacin in 102 normal women aged 17 to 35 years, 63 of whom were vegetarians; 100 pregnant women not suffering from any major complications of pregnancy were similarly studied. The duration of pregnancy at the time of study varied from two to nine months, and 60 of these women were vegetarians. A third group consisted of 29 pregnant women suffering from nutritional anemia. Estimations of urinary niacin, nicotinamide, nicotinuric acid, and trigonelline were made.

Most of the normal women did not excrete niacin in appreciable amounts. No significant difference was noted between the vegetarians and the nonvegetarians, although the intake of niacin was greater in the latter. The average excretion of nicotinamide in normal vegetarians was 1.1 mg. per day (range 0.01 to 9.6) and the value for nonvegetarians was 0.8 mg. per day (range 0 to 2.5). The average excretion of nicotinuric acid in normal subjects was 1.0 mg. and 0.7 mg., respectively, for vegetarians and nonvegetarians (range 0 to 6.0 mg. and 0 to 3.1 mg. respectively). Trigonelline was not detected in the urine in most of the normal subjects, vegetarian or nonvegetarian. The average value in those who did show trigonelline in urine was 0.1 mg. for vegetarians and 7.0 for nonvegetarians. The average excretion of N′methylnicotinamide was 3.5 mg. (range 0 to 9.8 mg.) in vegetarians and 3.5 mg. (range 0 to 9.0 mg.) in nonvegetarians. Larger amounts of this substance were excreted than any other nicotinic acid metabolite. Pregnant women were seen to excrete greater quantities of N′methylnicotinamide than nonpregnant women.

The excretion of total nicotinic acid metabolites showed a similar pattern. The values for excretion of both of these tended to rise with advancement of pregnancy. The excretion of nicotinamide during the second trimester was higher than that during the first trimester, but no further increase was seen as the pregnancy went on to term. No significant difference was noticed in the excretion values between primiparas and multiparas. In pregnant women with anemia greater quantities of total nicotinic acid metabolites were excreted than in normal nonpregnant women, but the value was less than that obtained in normal pregnant women. There was no difference in excretion between the vegetarian and nonvegetarian subjects in the group of normal pregnant women.

Hypertension.—S. Padmavati (*Journal of the Association of Physicians of India,* vol. 7, March, 1959) studied the incidence of hypertension in Delhi by estimating blood pressures in both high and low income groups and in the rural population. Thus 316 men and 35 women studied came from the high income group, 576 men were mill employees belonging to the poorer classes, and 383 men and 451 women were from rural areas. It was found that the systolic and, less markedly, diastolic pressures were much higher among the well-to-do. In the poorer classes there was no significant rise in blood pressure with age in men, a small but steady rise was seen in poor women, and a more marked rise with age was noticed in the well-to-do. A steady rise with increasing body weight was present in both groups. The poorer classes were underweight by western standards and the well-to-do were normal or slightly overweight and showed a steady rise in weight with age which was absent in poor men, who lost weight after the age of 40. Compared to figures from the United States the well-to-do subjects in this study had lower systolic pressures after the age of 30, but the diastolic readings were higher throughout. The poorer persons showed a lower systolic reading at all ages and a lower diastolic pressure only after the age of 50. The difference in the readings in the rich and poor might thus have been due to the low body weight in the latter, which might also explain the differences from western figures.

Data regarding the incidence of hypertensive disease were available from only 7 of the 16 Indian states and these, being mostly hospital statistics, did not truly represent the incidence in the country as a whole. A variation was seen in different states, Bombay giving the highest incidence. In the high income groups, whose members had the highest average body weight and higher average levels of normal blood pressure, the incidences of blood pressure readings over 140/90 mm. Hg and of hypertensive disease were the highest of all the three groups. The rural group came next and then the industrial. The incidence of blood pressure over 140/90 mm. Hg in American men in the fifth, sixth, and seventh decades of life has been reported by workers as 50, 60, and 70% respectively. The corresponding figures for India in low income groups were 7.8, 10.8, and 0 and for the higher income group 25, 0, and 85% respectively. As few people studied were in the seventh decade, the figures may not represent the actual incidence. The effects of hypertension on the vessels of the brain and on the heart varied in different localities. Thus cerebral hemorrhage was more common than heart failure in Agra, while the latter was predominant in Bombay and Lucknow.

R. V. Sathe recorded the blood pressure of 4,120 patients attending the outpatient department of J. J. Hospital, Bombay. Of these 125 showed hypertension, giving an incidence of 3.01%. Of the 2,362 men 48 or 2.03% and of the 1,758 women 77 or 4.3% had hypertension; 36 of the 125 patients with hypertension were studied in detail. Of these 27 had essential and 9 had secondary hypertension; 24 of the 36 were in the age group 40 to 59, 8 were between 20 and 39, and 4 were between 60 and 79 years. Four were lean, 20 had an average weight, and 12 were stout. Only three gave a history suggestive of hypertension in parents or relatives, others showing no evidence of any hereditary influence. Psychological factors seemed to be contributory in 9 of the 36 patients. Most were reported to have repressed rage, although outwardly they appeared gentle, poised, and well-meaning. Only one was outwardly irritable and hostile. Of the 36 there were 24 men and of these 13 were following an active and 11 a sedentary occupation. All the women were active. Of the nine patients with secondary hypertension six cases were due to renal disease, two to endocrine disorders, and one to arteriosclerosis.

K. N. Gour surveyed patients with hypertension in rural, semiurban, and urban areas and found an incidence of 0.15% in the rural areas, 0.64% in the semiurban areas, and 5.6% in the urban areas. A history of one or both parents suffering from hypertension was noted in 57.1% of the patients in his series; 97% were over 40 years of age, the maximum incidence being found in the age group 56 to 60. No patient with hypertension was below 35 years of age. It was also more common in men than in women, and 60% of the persons with hypertension were overweight.

UNITED KINGDOM

Campaign Against Respiratory Disease.—At a press conference held at the Central Middlesex Hospital, London, Dr. H. Joules, medical director of the hospital, called for a royal commission to inquire into the problem of chest diseases in Britain. He described the past winter as the worst in his 33 years of experience for the patient with chest disease. He drew a gloomy picture of the increasing toll of lives taken by bronchitis. In Newcastle-on-Tyne 36% of the men and 17% of the women over the age of 30 have evidence of the disease. The havoc wrought by cancer of the lung is threatening to undo all the advances in the treatment of tuberculosis. Coronary disease is also increasing at an unprecedented speed and has the effect of crippling the lungs of those it does not kill.

Dr. Joules listed as the main causes of chronic bronchitis (1) atmospheric pollution (especially by sulfur-containing gases), caused mainly by power stations and industry; (2) tobacco smoking; (3) dust and fumes from industrial plants; (4) influenza viruses, known and unknown, which damage bronchi and predispose to the growth of staphylococci; and (5) overcrowding in public vehicles at the rush hours, and the resulting transmission of microorganisms. Dr. Joules said that his 800-bed hospital ceased to be a general hospital during February and March. No operations were scheduled and the only admissions were those of patients with emergency chest and heart conditions. In February 286 such patients were admitted and 103 died. The figures for March were 333 and 93. On one Monday morning there were 23 deaths. In the first three months of the year the already swollen hospital waiting list had nearly 400 names added to it.

A general practitioner confirmed Dr. Joules' report. The hospital could not accept half his emergency cases. He thought that the time had come to attack air pollution with the same vigor as that with which the Victorians attacked water pollution 100 years ago. The hospital laboratory was overwhelmed with sputum specimens for culture in February and March. In 1958 600 resistant strains of staphylococci were cultured, and in the first three months of this year the figure was already 300. With patients harboring these organisms there was bound to be cross-infection in the surgical wards.

Dr. S. R. Craxford, of the Division of Atmospheric Pollution, Department of Scientific and Industrial Research, said that the average Londoner has a heaping teaspoonful of solid matter deposited in his lungs every year. In London there are 40 mg. of particulate matter per 100 cu. m. of air. This proportion rises to 200 or 300 mg. in periods of peak pollution. Dr. Joules resolved to take the matter before Parliament and urged an investigation by a royal commission. He pointed out that there are many vested interests to be fought, in particular those concerned with the production of electricity and coal gas and the transport and cigarette industries. Most important is the vested interest of the treasury in tobacco, from which it derives about 2 billion dollars a year in tax revenues.

Cardiac Team Goes to Russia.—A cardiac team from the London Postgraduate Medical School, Hammersmith Hospital, spent three weeks in Moscow where they demonstrated the Melrose heart-lung machine and the technique of elective cessation of the heart, both of which were developed in Britain, as well as methods of open-heart surgery. The team, headed by Mr. W. Cleland, a cardiac surgeon, included Dr. D. Melrose, inventor of the heart-lung machine; Mr. H. Bentall, a surgeon; Dr. A. Holman, a cardiologist; Dr. J. Beard, an anesthesiologist; Mr. J. Robson, a technician; and Miss Phyllis Bowtle, an operating room assistant. The team was invited to Moscow by Professor Bakulev, President of the Academy of Medical Sciences of the U.S.S.R. in the Institute of Thoracic Surgery.

During their stay in Moscow members of the team were guests of the Soviet government. Their transportation was paid by grants from the British Council, the Nuffield Foundation (which has been mainly responsible for financing the heart-lung machine in Britain), the Postgraduate Medical School of London, and three London teaching hospitals. Several pharmaceutical and instrument companies provided materials and instruments for the visit. A Melrose machine has been purchased by the Soviet government for use in Moscow. Mr. Cleland, who will be the first surgeon from the west to operate in Russia since before World War II, was commissioned to convey the good wishes of the Royal College of Surgeons to the Soviet Academy of Medical Sciences. He presented a set of textbooks and monographs on thoracic surgery to Russian surgeons.

Hydrocephalus.—Speaking at the annual convention of the National Society for Mentally Handicapped Children Mr. G. MacNab, surgeon at Westminster Hospital, London, described the work he and his co-workers have been doing on hydrocephalus. They studied nearly 200 children with this condition from infancy. Over 40% survived, with natural arrest of the hydrocephalus, and 42% had intelligence quotients of 85 or above. One-third of the children had meningomyeloceles, and in these it was common for inflammatory adhesions to block the cerebral aqueduct or the foramens of the fourth ventricle. In only 14 of 100 autopsy examinations was the hydrocephalus found to be due entirely to congenital malformations. Infection accounted for 47, hemorrhage for 24, and tumor for 4%, leaving 11 with the cause undetermined. Mr. MacNab treated about 30 hydrocephalic children by inserting in one of the ventricles the Spitz-Holzer valve, which was developed by an American engineer whose child was affected. This valve has a unidirectional flow and drains the cerebrospinal fluid into the superior vena cava at a set pressure of 50 mm. H_2O. The valve is siliconized to prevent the coagulation of the blood. This is the first successful technique for carrying cerebrospinal fluid directly into the blood stream. The cost of the valve is about $85.

Maximum Permissible Radioactive Contamination.—The report to the Medical Research Council by its Committee on Protection Against Ionizing Radiations was published in the *British Medical Journal* of April 11. An editorial in the same issue stated that permissible doses of radioactivity for workers under conditions of emergency or accident have been considered by the International Commission on Radiological Protection (ICRP) and agreed to although not yet formally published. No universally accepted permissible doses for an emergency affecting a population not occupationally exposed to radiation have been published, but doses are readily calculable and were in fact used as a guide to action in October, 1957, when a fire in the Windscale no. 1 reactor in Cumberland permitted the escape of volatile fission products into the atmosphere.

The committee considered that, for the population living at the scene of such an accident, the limiting hazard will generally be internal irradiation due to ingestion of local foods contaminated with fission products, rather than from inhalation. The radioactive cloud is nonpersistent, but any radioactivity deposited persists for varying lengths of time, depending on physical and biological phenomena. This may affect man indirectly through his dependence on grazing animals for meat or milk. Therefore this report deals with those fission products which are of high yield in fission, readily absorbed from the digestive tract, and, with the exception of the first, long-lived—namely, iodine-131, strontium-89, strontium-90, and cesium-137. Iodine and strontium are furthermore concentrated in particular tissues.

Although the permissible dosage of strontium-90 is discussed on the basis of the dosage of radiation that will result from the retention for many years in bone of a fraction of the amount ingested, the other radioactive isotopes are considered from the aspect of the total dose of radiation they will give during their whole life of several months in the various tissues. The report suggests levels which are intended to apply to small numbers of people compared with the whole population. In this respect it follows the principles of the ICRP's recommendations. The Medical Research Council's Protection Committee takes a new attitude toward strontium-90. The concentrations rated as permissible—1,000 strontium units (S. U.) for the occupationally exposed (the ICRP figure) and 100 S. U. for members of the general population—were based on the relative doses, for acute toxicity, given by the proportion radium-226: strontium-90=10:1.

There are now data to indicate that for chronic toxicity the ratio is about 50:1, which is what one would predict from the calculations of respective dosages. The committee has been consistent and has issued figures on the permissible dosages for strontium-90 as for other chronic radiation hazards on the dose-rate. It has followed the line of the ICRP, regarding for small populations 10% of the dose for the occupationally employed as the maximum permissible. This means 1.5 rads per year for bone cells. Under the worst conditions this is equivalent to the dosage from areas of bone contaminated at the level of 500 S. U.—that is, 500 $\mu\mu$c per gram of calcium. What the committee virtually says is that even small areas of bone can become contaminated to this level only when the intake reaches about 2,000 $\mu\mu$c of strontium-90 a day, on the assumption of a daily dietary intake of 1 Gm. of calcium, which is about the average normal for persons of all ages in Great Britain.

What could be surprising at first sight is that no distinction is apparently drawn between the infant or child in the environment and the adult. The distinction can be observed in practice rather than theory. The committee, taking into account the appropriate metabolic data, has calculated the maximum permissible daily intakes (in $\mu\mu$c per day) of each of these radioactive substances to obtain the maximum permitted doses to the tissues of infants, children, and adults. The obvious result is that the permissible intake increases with age, but the various articles of diet are not consumed in the same ratios by infants, children, and adults. For instance, the infant drinks as much milk as the adult and milk is the food most likely to set the limit. Therefore, in practice, concentrations of the respective radioactive substances in foods will be determined by the tolerance of the young.

Poliomyelitis Immunization.—The response of infants to poliomyelitis vaccine is governed by two factors, the level of maternal antibody and the number of antigenic stimuli given in the course of primary immunization. Perkins and co-workers showed that in only a small proportion of infants under 10 weeks of age can a satisfactory basal immunity be established by the injection of two doses of poliomyelitis vaccine (*Brit. M. J.* 1:680, 1959). They have made two further studies on the problem (*Brit. M. J.* 1:1083, 1959). The first, with 1-week-old infants, was designed to determine whether the inhibiting action of maternal antibody could be overcome by increasing the number and size of the dose; and the second, with 16-week-old infants, was made to determine whether infants of this age had reached a stage at which their immunological activity could overcome the inhibiting effect of passively acquired antibodies, and whether a more substantial basal immunity could be established by three doses rather than two. In the 1-week-old infants it was found that doubling the dosage from 1 to 2 ml. and giving two doses produced no better response than previously when two doses, each of 1 ml., were given. On the other hand three doses, each of 2 ml., produced a better response; but even with this schedule there was a high proportion of nonresponders to all three viral types, particularly type 1, even among those infants possessing maternal antibody.

More encouraging results were obtained with the 16-week-old infants. With those who had little or no maternal antibody the response to two doses, each of 1 ml., was no better than had been obtained in a previous study with 10-week-old infants on a similar schedule. On the other hand, three doses gave a decided improvement, 83% of the infants responding with type 1 and all with types 2 and 3 antibodies. The geometric mean antibody titers reflected the greater immunizing power of the three-dose schedule. The true picture will only be seen after a year, when a booster dose will be given to all the infants. In the meantime it is suggested that in the state of our present knowledge immunization should be delayed until the age of 6 to 9 months, when three doses of vaccine should be given.

Taste Response to Phenylthiocarbamide.—Some people taste phenylthiocarbamide (PTC) and others do not. This bimodal taste response is an example of human genetic polymorphism. As PTC is a known goitrogen, Kitchin and co-workers have tested the taste response to it of patients with thyroid disease and compared the results with those of normal subjects (*Brit. M. J.* 1:1069, 1959). A series of 447 patients who had undergone thyroidectomy and whose thyroid status was known were tested with PTC. In addition 15 patients were tested before and after thyroidectomy to determine whether any change occurred in the taste threshold. A control group of 265 subjects was composed of hospital nurses and university students. In 246 patients with adenomatous goiter a significantly high incidence of nontasters was found, and this was proportionately greater in men than women. In 133 patients with toxic diffuse goiter a significant excess of PTC tasters was found but without sex difference. There was practically no change in the taste threshold after thyroidectomy. The findings suggest that the taster/nontaster genotypes are of importance in determining the type of thyroid disease that may develop. From a biochemical standpoint the differential taste response is confined to substances with the grouping $-N-C{=}S$, and their biological action is to inhibit tyrosinase and the synthesis of thyroxine. This effect occurs within the thyroid, is uninfluenced by treatment with iodine, and results in thyroid hyperplasia under the stimulus of pituitary thyrotropin.

Goitrogenic substances allied to PTC occur in vegetables of the brassica type, which are fed raw to cattle in the winter. Goitrogens have been isolated from cows fed on kale, and it has been suggested that cow's milk could be an important source of goitrogens in man. This would occur only in winter, as in the spring and summer the cows would be grass-fed. If this were so, cycles of seasonal involution and hyperplasia would occur in the thyroid, particularly in nontasters of PTC, and it is just this pathological sequence that is known to give rise to adenomatous goiter in later life.

Metabolites of Phenylbutazone.—The relatively high incidence of gastrointestinal side-effects resulting from the use of phenylbutazone in rheumatic and bone disorders has led to increased efforts to find a derivative that would be better tolerated, without significant reduction in activity. Hart and Burley reported the results of a trial with a metabolite of phenylbutazone, "metabolite I," or G.27202, which is the parahydroxy- derivative (*Brit. M. J.* 1:1087, 1959). This is one of two metabolites isolated from the urine of patients undergoing treatment with phenylbutazone. Preliminary studies showed that G.27202 was as potent an anti-inflammatory agent as phenylbutazone but was less ulcerogenic. Both drugs were given to patients with rheumatoid arthritis, ankylosing spondylitis, osteoarthritis, psoriatic arthropathy, osteitis deformans, and Reiter's syndrome. The object of the trial was to see if G.27202 was as effective as phenylbutazone and whether it caused less gastric irritation. The patients were given both drugs in the same dosages for one to three weeks, unless gastrointestinal symptoms necessitated discontinuing treatment.

Fourteen patients received the drugs for 3 to 12 months. Patients were asked which drug was the more effective in relieving their pain and stiffness, what side-effects were experienced, if any, and the extent of fluid retention. G.27202 caused much less gastric irritation than phenylbutazone. Although long-term studies may reveal a larger number of side-effects, these were infrequent and mild with a daily dose of 100 to 600 mg. taken orally with meals; but G.27202 appeared to have less analgesic activity than the parent substance. The ratio of their activities was about 2:3. This reduction in effectiveness, however, only slightly offset the more definite reduction in gastric irritation. G.27202 is slowly metabolized, and there are distinct advantages in using a slowly metabolized, long-acting substance in the treatment of chronic rheumatic disorders. The authors considered that G.27202 might play a useful part in treating patients who tolerate phenylbutazone poorly.

Toxoplasmosis in Sheep.—Toxoplasmosis is more prevalent in Britain than was formerly thought. In man it causes severe congenital brain damage and is a common cause of posterior uveitis. Attention is being directed to the source of human infection. Rawal (*Lancet* 1:881, 1959) found Toxoplasma in sheep. The serum of 11% of live sheep gave a positive reaction to the dye test for toxoplasmosis. Samples of blood serum and brain were removed from sheep in the abattoir, and 21% of the serums showed a positive reaction to the dye test for toxoplasmosis, at a titer of 1:4 or more. An extract of the brains was inoculated peritoneally into mice and their brains examined six to eight weeks later. About 20% of the sheep brains produced antibodies to Toxoplasma in the inoculated mice and 29% produced cysts in the brain. Toxoplasmosis could arise in man from eating the meat of infected sheep, but only if it were not properly cooked.

CORRESPONDENCE

SYNDACTYLISM AND POLYDACTYLISM

To the Editor:—Authors persist in stating that syndactylism is the commonest congenital deformity of the hand. This statement appears in the latest edition of Bunnell's Standard textbook, "Surgery of the Hand" (ed. 3, Philadelphia, J. B. Lippincott Company, 1956); in Barsky's "Congenital Anomalies of the Hand and Their Surgical Treatment" (Springfield, Ill., Charles C Thomas, Publisher, 1958); and in the just-published "Orthopaedics: Principles and Their Application" by Turek (Philadelphia, J. B. Lippincott Company, 1959). This contention is not borne out by a survey of congenital anomalies as recorded on birth certificates in Pennsylvania covering the years 1951-1955, inclusive, which indicates that polydactylism of the fingers is the most frequently recorded of all congenital anomalies, with a total of 703 cases. In contrast to this, only 85 cases of syndactylism of the fingers were recorded in the same period, a ratio of more than eight to one. Even allowing for errors in diagnosis and failures in recording by the physician attending the birth, this discrepancy is too great to be ignored.

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SUBLUXATION OF HEAD OF RADIUS

To the Editor:—In his article entitled "Subluxation of the Head of the Radius in Young Children" in The Journal, April 11, pages 1734-1736, Dr. Hart does not mention why this frequently occurring condition is sometimes overlooked, namely, that the pain may be felt at the distal end of the radius instead of at the elbow and that this draws attention away from the real site of the lesion.

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To the Editor:—I was pleased to read the article by Dr. Hart, in The Journal, April 11, on subluxation of the head of the radius in young children. Years ago, when I was in general practice, I felt that the condition we called "pulled elbow" should have been called to the attention of our colleagues. It is a painful and disabling condition, and usually the gentle manipulation incidental to a careful examination and palpation corrects the defect, with the familiar clicking sound mentioned in Dr. Hart's article. It is interesting to have his explanation, since 50 years ago we did not have access to x-ray at every occasion.

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THE LEISURE CORNER

HORSEMANSHIP

The art of horsemanship has attracted the interest of many physicians. The fact that in riding a horse one deals with a live animal that has nerves and susceptibilities, fancies and fears, and a character of its own as definite as that of the rider provides one of the great charms of this sport. The rider must execute many varied muscular actions simultaneously, and these have to be carried out in unison with unforeseen movements of the horse. Indeed, the rider and the horse have a mutual language of infinite vocabulary that establishes harmonious communication.

The quick changes of the mood of the animal must be comprehended and responded to in a manner suited to the given moment. That is why it is impossible to establish too many rigid rules. It is more or less the direct relationship that arises between rider and his horse that holds the secret of the art of horsemanship. The use of the fingers and hands on the reins and the conveyance of numerous communications to the horse through signals received in its mouth comprise a code of what might be called muscular words; this is a subtle and intricate language known as "hands." In turn, "hands" may be supplemented by "aids," which are movements of the rider's legs and body. Such communication is not as simple as may be supposed. It can be loosely compared to a dumb alphabet, containing many variations in intensity and shading. To a large extent the employment of this form of communication depends on the rider's ability to read his horse's inclinations and emotional responses and to interpret its actions, so that both rider and horse may work in conjunction with no serious misunderstandings. A good horseman rides with his brain more than with his muscles. One test of this is the decision of whether the rider remains in the saddle or not, a decision resting entirely on the manner in which the rider "converses" with his horse.

Since a horse does not reason in the accepted sense of the word, the animal will sometimes shy because of fear or its inability to respond to the rider's cerebral processes. Occasionally a horse will jump away from objects crossing its path, dashing past them or even turning around. Although the animal usually shies as the result of fear, this is sometimes prompted by defective sight or by an unskilled rider who, being nervous himself, conveys his own fear to the animal. Shying is sometimes due to a horse's being tense, in which case it is likely to be startled by a sudden noise. As a rule, a remonstrance and a pressure of the rider's legs on the horse's body should be sufficient to reassure the animal. If not, a smart trot or canter will often serve the purpose.

When a horse is frightened, punishment cannot fail to do more harm than good, and it generally spoils the horse. When a horse attempts to turn around in its refusal to obey an order, it should be promptly stopped. However, if the horse cannot be stopped, it should be made to complete the circle of movement and then again coaxed to pass the object that made it shy in the first place. The horse should be encouraged to approach the object of its suspicions and sniff at it until there is reassurance that there is no danger. An encouraging phrase is of considerable value at such a time in allaying a horse's timidity. Horses inclined to shy are more likely to do so when handled by riders who use slack reins, because they lack confidence in the rider. A horse's fear, to a certain extent, can be lessened by a firm hand on the reins.

An important rule of the road is that a rider must keep to the right, except when he wishes to pass. In this instance, he passes on the left, just as in driving an automobile. However, the line of progress for a rider ends with this comparison. An automobile, with its powerful brakes and its ability to make sharp turns, can not only be stopped abruptly within a comparatively short distance from an object but also be made to swing out in order to pass it. This is not possible with horses on a bridle path or a smooth, surfaced road. Any movement requiring a sharp turn is to be avoided. A horse should begin a pronounced turn sooner, and then take a more gradual course. It must begin to bear to the left at a sufficient distance from the obstacle to allow a smooth, graduated line.

The horse is aware of each movement made by its rider. Every action of the arms, legs, feet, and head of the rider are seen by the horse. The eyes of a horse are situated at the sides of its head, almost in the position of a human being's ears. This anatomic feature provides the horse with a wide range of vision; it can see what is behind as well as what is in front. With the eyes placed where they are the horse is to a limited extent guarded against a stalking enemy; but the fact that each eye has a separate and complete range of vision does not make it easy for the animal to combine the vision of the two eyes. While a man's two eyes furnish a direct range of vision in front of him and extending to both sides, a horse has to deal with two separate views, each independent of the other.

Properly performed, riding promotes increased suppleness and grace of movement. In addition, in an age in which the automobile has become a substitute for exercise, it is a healthful pastime. Men and women who have spent a lifetime acquiring self-control, self-reliance, patience, and accuracy, as well as other qualities with which physicians are familiar, are often pleased to know that in the art of horsemanship these attributes can be successfully expressed.

MEDICOLEGAL ABSTRACTS

Autopsies: Performance Without Widow's Consent.—The plaintiff, now deceased, sued the defendant city for damages for the alleged mutilation of the body of her deceased husband. From a judgment for the plaintiff the defendant appealed to the Supreme Court of Michigan.

The husband's death occurred as a result of a traffic accident on a public street in Detroit involving a bus owned and operated by the city. After the accident his body was removed to a city hospital where an autopsy was conducted. In the course of the autopsy certain organs were removed and sent to a laboratory for the purpose of determining the presence or absence of alcohol therein. This examination resulted in the destruction of the organs.

At the trial it appeared that the autopsy had been performed by the medical examiner of Wayne County. The defendant's physician and surgeon was present at the autopsy, however, and the organs in question had been removed at his request, not because the medical examiner thought the removal necessary. At no time did the plaintiff consent to the removal.

On appeal two issues were raised: Was the widow entitled to damages because of the unauthorized autopsy, and did her cause of action for damages terminate when she died?

The great weight of authority holds that the unlawful and intentional mutilation of a dead body gives rise to a cause of action on behalf of the person or persons entitled to the possession, control, and burial of such body. The plaintiff therefore stated a cause of action in the widow's favor and the proofs introduced on the trial tended to support the pleadings. No inquest was ordered by proper authority, said the court, and it appears from undisputed testimony that the defendant's medical representative, present at the autopsy, requested the medical examiner to remove certain organs from the body and that the action was taken pursuant to such requests, although the examiner did not deem it necessary.

Did this cause of action survive the death of the widow? In our opinion, said the court, and in accordance with general principles of law recognized in prior decisions, the widow's cause of action did not survive her death. It ceased to exist at the time of death and was not subject to revival by the administrator of her estate. The right that the defendant was charged with having violated was purely personal in character. It did not involve an injury to person or property within the meaning of the survival statute, and it was not of such character as to survive at common law. The judgment for the plaintiff was accordingly reversed. *Deeg v. City of Detroit*, 76 N. W. (2d) 16 (Mich. 1956).

MEDICAL FILM REVIEWS

Nursing Care with a Stryker Frame: 16 mm., black and white, sound, showing time 14 minutes. Produced in 1958 by the Department of the Army. Procurable on loan from Armed Forces Institute of Pathology, Walter Reed Army Medical Center, 6825 16th Street N.W., Washington 25, D. C.

This film first depicts the various components of the Stryker frame, including the foundation cart, the overhead metal bar, the utility tray, the posterior frame, the anterior frame, the face support, the foot support, and the three turning straps. It then describes the nursing techniques required in operating the frame, including transferral of patient from bed or litter to frame, placing of foot support, placing of pillows and arm rests, insertion of bedpan, checking of important locking springs and wheel locks, and turning of patient with and without drainage tubes. The emphasis on informing the patient and on his comfort and safety is valuable, and the initial listing of instructions for the use of the frame and its assemblage are helpful. The summation of the key points in the film is excellent. This film is recommended for showing to nursing groups who are interested in the use of the Stryker frame.

The Return: 16 mm., black and white, sound, showing time 39 minutes. Produced in 1958 by MPO Productions, New York, under a grant from the Office of Vocational Rehabilitation. Procurable on loan or purchase ($140) from American Physical Therapy Association, 1790 Broadway, New York 19.

This film was produced primarily to interest young people in the profession of physical therapy. It depicts the human and dramatic side of rehabilitation through the story of a youthful paraplegic who was injured in an auto accident. It is a gripping film portraying both the accident to the paraplegic and his subsequent rehabilitation, and shows some of the daily work activities of the physical therapist. However, it would seem to be more of a "case history" of the paraplegic than a portrayal of the over-all training and responsibilities of the physical therapist. The film is bound to have an emotional impact on the viewer because of the dramatic situation which is developed, but it is regrettable that it does not include more information about the physical therapist's educational program and the great diversity of types of patients she will encounter. This film can be recommended to the following groups: those interested in a review of a rehabilitation program for paraplegics; any group which the user is interested in encouraging to support or contribute to a rehabilitation service or center in a community; and prospective physical therapy students, in order to show them one portion of the work of the physical therapist.

A New Chapter: 16 mm., black and white, sound, showing time 28 minutes. Produced in 1958 by Dynamic Films, New York, for and procurable on loan from Smith Kline and French Laboratories, 1530 Spring Garden Street, Philadelphia 1.

This film presents the story of how Ben, a young man who had been confined to a mental hospital for three years, meets the problems of his first weeks of life outside the institution. Ben is at first overprotected by Frank, his commiserative older brother, received in hovering silence by his family, welcomed back too effusively by his church, and refused employment even when he musters the courage to seek it. His family physician reassures Ben that he is "not sick," but immediately sounds one of the few discordant notes in the film by stressing the importance of the continued taking of medicaments. Ben eventually discards the temptation to return to the hospital as an escape from such stresses, and the film closes in the hopeful expectation that he will readjust to the realities of family, work, and society. The pamphlet accompanying the film recommends its use to stimulate discussion among psychiatric patients, or in groups of laymen who might aid or employ them after discharge. For the former purpose the film overplays the tenderness most patients can realistically expect, whereas prospective employers and others should not be led to anticipate that many ex-patients will resemble the handsome, well-spoken, intelligent young Hollywood type who plays Ben. Nevertheless, there are no seriously misleading or oversentimentalized episodes in the script, and the film's pictorial clarity and quietly modulated sound help to commend it to most viewers. Any ensuing group discussion, however, should be conducted by an expert who could adapt it to specific audiences.

NEW FILM ADDED TO A. M. A. MOTION PICTURE LIBRARY

Kielland's Midwifery Forceps: 16 mm., color, sound, showing time 15 minutes. Prepared in 1956 by Alistair Gunn, M.D., London. Procurable on loan (service charge $3) from Motion Picture Library, American Medical Association, 535 N. Dearborn St., Chicago 10.

In this film the Kielland midwifery forceps are described and demonstrated. The careful and exact diagnosis of the position of the occiput by abdominal and pelvic examination was emphasized by Kielland, and these methods of examination are depicted at some length. The delivery of an emergency case with labor delayed owing to arrest of the head in the transverse diameter is demonstrated. The forceps are applied by Kielland's classic method. This is an excellent film depicting the use of the Kielland midwifery forceps with a classic application of the anterior blade and its intrauterine rotation in a woman with arrest of labor in R. O. T. The film is straightforward, direct, and to the point, and teaches the lessons of the Kielland forceps well. It is highly recommended for obstetricians, general practitioners, residents, and interns.

MEDICAL LITERATURE ABSTRACTS

INTERNAL MEDICINE

A Statistical Study of 1000 Cases of Leprosy Observed in Rangoon for Approximately Two Years. R. A. Lewis and R. Edwards. Internat. J. Leprosy 26:236-251 (July-Sept.) 1958 [New Orleans].

Leprosy is widely prevalent in Burma. According to a recent inquiry there were 3,035 segregated cases, 21,379 unsegregated cases, and an estimated 75,000 unknown cases, or a total of approximately 100,000 in a population of 17.5 million. In view of the scanty information and conflicting opinions regarding the character of leprosy in Burma, 1,000 cases were studied at the special skin clinic of the Rangoon General Hospital. The data were transferred to punch cards, analyzed, and tabulated. Analysis of the distribution of types of leprosy revealed that 45% had the tuberculoid, 23% the indeterminate, and 32% the lepromatous form of leprosy. The disease was most frequently noted by individuals of the 10-14 age group, although those in the 20-24 group came to the clinic in greatest numbers. The tuberculoid type of leprosy occurred earlier than the others, and the history was shorter. In all types the percentages of patients with deformity increased with increase of age and duration of illness. The incidence of leprosy in Rangoon and environs was highest among Indians and next among Muslim-Burmese; it was less among Burmese and least among Chinese. Between the ages of 12 and 60, leprosy was much more common in males than in females, the disproportion being most marked in lepromatous cases. In the latter type, the frequency of deformities was also greater in males than females. Children had a higher proportion of tuberculoid and a lower frequency of lepromatous cases, and a much lower deformity rate. Under treatment the proportion of patients reaching an inactive stage was considerably higher among children than adults.

Results of treatment with diaminodiphenylsulfone (DDS) were influenced by the age of the individual and the duration of the disease. In tuberculoid cases with deformities or with reactions, the efficacy of treatment was lessened. In lepromatous cases the occurrence of reactions interfered with improvement in the clinical condition and bacteriological status, as did irregularity of treatment. One-third of all cases reached an inactive stage, with faded lesions in tuberculoid and indeterminate cases, or negative smears for a year in those of the lepromatous type. The bacteriological status of lepromatous cases improved in 87.2%, remained stationary in 12.2%, and deteriorated in only 0.6%. From the public health viewpoint, early diagnosis and treatment, especially in children, are stressed.

SURGERY

Transcranial Yttrium 90 Hypophysectomy. J. P. Evans, W. Fenge, W. A. Kelly and P. V. Harper Jr. Surg. Gynec. & Obst. 108:393-405 (April) 1959 [Chicago].

The authors describe their experiences with transcranial radioyttrium (Y^{90}) hypophysectomy in 31 patients with carcinoma of the female breast. At first they tried to destroy the hypophysis with 4 properly placed radioactive pellets of 0.5 to 1.0 mc. each. It became increasingly evident that accurate placement was difficult, and on a few occasions beads were actually deposited outside the sella. It was concluded that destruction of the gland would probably be increased by the use of an increased number of point sources of lesser activity. Initially, the exposures were made through a standard frontal craniotomy on the right. The insertion of a lumbar catheter for drainage of the cerebrospinal fluid facilitated exposure and lessened trauma to the frontal lobe attendant upon retraction. A satisfactory exposure could be made through a crown trephine opening. But while the authors attempted to perfect the transcranial approach, the transsphenoidal Y^{90} attack was developed by a colleague in the otorhinolaryngologic department. Since the transsphenoidal Y^{90} hypophysectomy had a lower mortality rate than the transcranial, it proved a more readily acceptable procedure at the University of Chicago Clinics to both the referring physician and the patient.

The follow-up study of 15 months presented here is concerned only with the results of transcranial Y^{90} hypophysectomy. This procedure has been followed by an arrest of breast cancer in 8 of the 31 women of 12 or more months' duration. In 3 cases a regression of the disease process has persisted for

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The place of publication of the periodicals appears in brackets preceding each abstract.

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13 months. Transcranial Y^{90} hypophysectomy approximates surgical hypophysectomy in safety and in effectiveness in the treatment of mammary cancer.

Although transsphenoidal Y^{90} hypophysectomy is now preferred to the transcranial method, comparison of the complication rate of the transsphenoidal approach with that of the transcranial must await detailed analysis of the transsphenoidal series. The percentage of gland destruction achievable by the transsphenoidal route likewise must await detailed analysis. It seems probable that total destruction of the gland is not imperative for favorable response in cancer of the female breast. Other factors in the total equation, and primarily endocrine gland dependence, are weighty considerations. The authors cannot state whether total destruction of the gland would produce a more lasting regression. They know of no method at present by which to predict which of the female breast cancers are hormonally dependent.

Effect of Yttrium 90 on the Pituitary Body, on Adrenal Glands, and Its Repercussion on the Thyroid Gland. E. Zanella, A. Peracchia and F. Fesani. Minerva med. 50:249-255 (Jan. 31) 1959 (In Italian) [Turin, Italy].

Small rods of radioyttrium (Y^{90}) were implanted through the nostril into the anterior lobe of the pituitary body of 2 patients, aged 70 and 77 years, one with prostatic and the other with mammary carcinoma, and with metastases in both instances. One patient died 4 days and the other 60 days after the implantation of Y^{90}. Autopsy revealed that necrosis of the tissue involved two-thirds of the anterior lobe of the pituitary, extending from 4 to 6 mm. around each Y^{90} rod, which area was encompassed by a region of newly formed connective tissue, 1 to 2 mm. in thickness. It is also probable that Y^{90} permanently inhibited the function of the nonnecrotized cells. No anomaly was observed in the vascular and nervous structures around the pituitary body.

Thyroid glands had diffuse nodules filled with eosinophilic colloidal substance and condensed collagen tissue in the peripheral sections. Adrenal glands were lighter in weight and had a thinner cortex than normal glands. The cell elements of the medulla presented regressive processes. The pathological changes of the thyroid and adrenal glands were more pronounced in the patient who died 2 months than in the other who died 4 days after the implantation of Y^{90}. Implantation of Y^{90} into the pituitary body is less hazardous than surgical hypophysectomy. It is also superior to surgery in the sense that, at least for 4 months, no cell particles of the pituitary seem to be left behind, which might regenerate and partially resume the function of the gland.

Complicated Cerebral Palsy: Surgical Pathologic Aspects. S. Rosner. J. Internat. Coll. Surgeons 31: 315-322 (March) 1959 [Chicago].

The author describes the postmortem and the surgical pathological picture in patients with complicated cerebral palsy, which may be defined as cerebral palsy associated with epilepsy, mental deficiency, or both. The brains of 51 children with cerebral palsy thus complicated were studied at craniotomy. Cerebral venous angioma of the sylvian fissure was observed unilaterally in 49. The remaining 2 patients showed, respectively, a subarachnoid cyst compressing the 4th ventricle and premature closure of the fontanels.

Five of the 51 patients, who ranged in age from 9½ months to 7½ years, came to autopsy. Their brains were examined both grossly and microscopically. In 4 a unilateral cerebral angioma near the sylvian fissure was observed. These observations were consistent in the 51 patients subjected to craniotomy. Specimens from the affected side were examined from the frontal, parietal, occipital, and cerebellar aspects. There was no evidence of porencephaly. These observations convince the author that venous angioma in the region of the sylvian fissure tends to cause changes in the encephalon that may be, to some extent, reversible; therefore, surgical removal of the pathological tissue should give the child a chance for recovery. Improvement in some respects was noted in all children who survived.

Ventriculo-Venous Shunt Using the Holter Valve as a Treatment of Hydrocephalus. K. W. Carrington. J. Michigan M. Soc. 58:373-376 and 383 (March) 1959 [St. Paul].

The author calls attention to the renewed interest in hydrocephalus in the last decade, particularly since the availability of various plastic materials. After citing the Matson procedure which consists in a subarachnoid–ureterostomy, he mentions various attempts to achieve ventricular decompression by means of ventriculovenous shunts. These shunts require the introduction of an artificial valve between the cerebrospinal fluid pathways and the venous system in such a fashion as to permit only unidirectional flow of fluid. The first reported use of such a valve was that of Nulsen and Spitz. For the last 3 years Spitz and Nulsen have been successfully utilizing a valve designed by John Holter. The Holter valve consists of a pair of "fish-mouth" type valves connected by a siliconized-rubber cylinder. This mechanism measures approximately 5 cm. in length and 6 mm. in diameter. The cylinder can be shortened, if desired, for very small children. The valves allow only unidirectional flow of fluid and are regulated at the time of manufacture to open at pressures greater than either 10 mm. or 50 mm. of water. The low-opening-pressure valves (10 mm.)

are used in children with myelomeningoceles and in patients with very pliable heads. The high-pressure valves (50 mm.) are used in all other patients. The valve is placed between 2 catheters, one to be placed in the lateral ventricle of the brain and the other in the right auricle of the heart.

The author presents an analysis of 50 cases in which ventriculovenous shunts were carried out on the neurosurgical service of the University of Michigan Medical Center. The patients ranged in age from 8 days to 12 years. All were followed for from 2 to 18 months after the cerebrospinal fluid had been shunted from the lateral ventricle to the right auricle by way of the internal jugular vein with the aid of the Holter valve. Sixty operative procedures were required in the 50 patients. These included 10 revisions in 8 patients. Eight revisions were necessary for internal jugular thrombosis or a plug in the distal catheter; in the remaining 2 a plug was present in the proximal catheter. At the time of this report 43 of the 50 patients had functioning shunts. Three patients died as the result of septicemia from 1 to 3 months after operation. These are regarded as surgical deaths (6%). Sixty per cent of the patients showed physical or mental improvement after the shunt. The shunt is recommended in patients with myelomeningoceles, since it may reduce pressure on the myelomeningocele sufficiently so that direct attack on the latter may be avoided.

The ventriculovenous shunt with the Holter valve is an attempt to return excess cerebrospinal fluid to the blood stream. The advantages of this procedure, as compared with other available methods, are: (*a*) preservation of the cerebrospinal fluid by returning it to the blood stream without loss of electrolytes; (*b*) no necessity to sacrifice any organ to carry out the procedure (as removal of the kidney in the Matson procedure); (*c*) little chance of ascending infection through the tube, with resulting meningitis, as the distal tube is in a sterile area; and (*d*) no alteration in technique required in treatment of either communicating or obstructive hydrocephalus.

Anomalous Drainage of Entire Pulmonary Venous System into Left Innominate Vein: Clinical and Surgical Considerations. D. A. Cooley and H. A. Collins. Circulation 19:486-495 (April) 1959 [New York].

Total anomalous drainage of pulmonary veins is a complicated and serious congenital cardiac anomaly. Usually prognosis is poor, and until recently complete surgical correction was not possible. Drainage of the entire pulmonary venous return from the lungs into the left innominate vein is the most common type of such anomaly. The authors report on 5 boys, between the ages of 2 months and 8 years, one 40-year-old man, and one 1-month-old girl with this type of anomaly, whose clinical features are described. All the patients were operated on. The 40-year-old man underwent exploratory thoracotomy and died during exploration. The 2-month-old boy underwent anastomosis of the vertical anomalous vein to the left atrial appendage and partial ligation of the vertical vein, and the female infant had the same operation performed; both these infants died 2 and 4 hours, respectively, after the operation. The 4 remaining boys underwent complete correction of their congenital cardiac anomaly during cardiopulmonary bypass. With the left atrium widely opened, an ample incision was made parallel to the direction of the common pulmonary vein behind the heart. In order to obtain the largest possible anastomosis, the incision was continued into the right atrium. Finally a transverse incision was made in the venous trunk, and an anastomosis was created between the trunk and the posterior atriotomy. On completion of the anastomosis, the atrial septum was transposed ventrally and sutured in such a manner that the left atrial cavity was increased in size. The right atriotomy was then closed. The pulmonary circulation was restored to an essentially normal anatomic state by the final step consisting of intrapericardial ligation of the vertical anomalous vein. Excellent results were obtained with this surgical technique in all 4 patients.

Interatrial Communications: On the Basis of 81 Cases. P. Soulié, J. Carlotti, F. Joly and others. Semaine hôp. Paris 35:669-708 (Feb. 28) 1959 (In French) [Paris].

The existence of an interatrial communication unaccompanied by other cardiac anomalies was demonstrated in 68 of the 81 patients whose cases are analyzed in this study. The other 13 patients, included solely for purposes of comparison with the first group, had interatrial communications associated with mitral stenosis in 3 instances and with anomalies in the pulmonary venous return in 10. Each of the 81 patients was given a complete clinical, radiologic, electrocardiographic, and hemodynamic examination. A vectorcardiographic study was made in 16 cases, and in 5 others cardiovascular catherization was repeated twice.

Functional tolerance of the septal defect in the 68 patients on whom the study is based was good: more than one-third of the patients were scarcely inconvenienced or showed no functional signs. The contrast between the functional latency and the importance of the objective signs of cardiovascular involvement was surprising; enlargement of the heart was radiologically evident in 4 of the 9 patients in whom the septal defect was perfectly tolerated, and 8 of the 9 had large arteriovenous shunts. Cyanosis is associated with pulmonary arterial hypertension and an increase in pulmonary resistance. It appears in most cases at a late stage as an ordinary sign of cardiac insufficiency, suggesting peripheral stasis rather than shunt inversion. It is rarely seen in young patients without heart failure, but when it is, it indicates a massive venoarterial shunt. Heart failure in patients with an interatrial communication is distinguished by the persistence, usually, of an exclusively or predominantly arteriovenous shunt and by the fact that arterial pulmonary hypertension may or may not be present. The pronounced elevation of the filling pressure of the right ventricle accompanying heart failure in these patients does not necessarily indicate myocardial failure.

Radiologic changes in the pulmonary arterial tree are a highly reliable sign of interatrial communication. The heart is constantly enlarged in patients in whom a large pulmonary output is associated with pulmonary arterial hypertension. Pulmonary arterial calcifications are rare, but when they occur, they seem to be a reliable sign of strong hypertension in the lesser circulation. The electrocardiographic signs are acquired anomalies which may regress rapidly after operative repair of the septal defect. They seem in the final stage of their development to be represented by a complete right bundle-branch block.

Hemodynamic exploration brought out the following facts: 1. The pulmonary venous saturation is normal in most cases. 2. Mixed shunts are present in more than half the cases. Study of the pressure curves recorded simultaneously in the 2 atria shows that the play of the pressures in the atrial phase does not suffice to explain the direction of the shunts. 3. Pulmonary arterial hypertension is frequent (about half the cases) but usually moderate. It is dependent on 2 factors: (1) an increase in pulmonary output, which leads to slight to moderate hypertension, and (2) an increase in pulmonary arterial resistance, which leads to strongly hypertensive manifestations. These 2 factors may be associated, the increase in resistance being in most cases an acquired phenomenon.

Comparison of the clinical, radiologic, electrocardiographic, and hemodynamic data shows that patients with interatrial communications can be divided into 3 major groups, each representing a stage in the development of the condition. The duration of each stage seems to depend on several factors: the size of the interatrial communication, the varying tolerance of the pulmonary vascular bed for arterial hypertension and increased output, and other individual variables. The average age of the patients increases from stage to stage; nevertheless, some patients may remain in stage 1 even after the age of 40 years. Surgical repair of the septal defect during the first 2 stages is preferable, but operation may be indicated in stage 3 patients with progressively increasing heart failure. Excellent postoperative results were obtained in one such patient operated on at the age of 45 years.

Angiosarcoma in Post-Mastectomy Lymphoedema: A Report of 5 Cases and a Review of the Literature. E. M. McConnell and P. Haslam. Brit. J. Surg. 46: 322-332 (Jan.) 1959 [Bristol, England].

The authors report on 5 women, between the ages of 41 and 53 years, who had undergone radical mastectomy for carcinoma of the breast. This was complicated a short time after the operation by the development of a persistent lymphedema of the ipsilateral arm. A highly malignant lymphangiosarcoma developed after a cancer-free latent period of 8 to 10 years in the edematous upper extremity of 3 of the 5 patients. It started as a solitary, purplish-red, subdermal, slightly raised, macular or nodular lesion, shortly followed by similar satellite tumors. Larger lesions became necrotic and cystic. Two of these 3 patients, who presented undoubted examples of the fully developed Stewart-Treves syndrome, died. One of them received palliative treatment (2 of the nodules had been excised); the arm was amputated in the other patient, but recurrent tumors had grown rapidly covering the left side of the chest wall. A fore-quarter amputation was performed on the third patient, and during the next few months there was no evidence of recurrence. Of the remaining 2 patients, one showed moderate vesicles and bruising in the edematous arm which remained unchanged for 3 years; the other patient had 3 small subcutaneous nodules, 1 of which remained unchanged for several months, while the other 2 regressed. These 2 patients were considered as examples of a "premalignant" phase in the development of angiosarcoma. In the light of present limited knowledge of this condition, it was felt that active radical treatment was not justified, and the patients have been kept on close follow-up.

Twenty-three cases similar to those of a highly malignant lymphangiosarcoma first described by Stewart and Treves in 1948 were collected from the literature; the patients were treated either by radiotherapy or by amputation of the arm. Examination of biopsy specimens obtained from 3 of the 5 patients in the authors' series revealed that the small subcutaneous nodules and "bruises" corresponded histologically with multifocal foci of endothelial proliferation, involving both lymphatic and blood vessels. Examination of the amputated arms of 2 of these patients and the autopsy performed on one of them showed that this premalignant angiomatosis is followed by the development of frankly malignant angiosarcoma occurring usually within a few months. The prognosis of postmastectomy angiosarcoma is very bad, its multifocal origin leading to a rapid local spread and metastasis occurring early by way of the blood stream. Long-standing lymphedema rather than a malignant diathesis is probably the important causative factor. Atrophy and degeneration, particularly of collagen but also of fat, can give rise to malignancy, and it seems possible that the long-continued degeneration resulting from the severe lymphedema may stimulate the development of a malignant connective-tissue lesion.

Ethylene Oxide Sterilized, Freeze-dried Dura Mater for the Repair of Pachymeningeal Defects. H. L. Rosomoff. J. Neurosurg. 16:197-208 (March) 1959 [Springfield, Ill.].

In the search for an ideal material with which to repair defects of the dura mater, metal foils (gold, silver, nickel, aluminum, platinum, stainless steel, tantalum), biological tissues (fascia lata, periosteum, peritoneum, fat), nonviable membranes (amnion, allantoic membrane, Amnioplastin, Cargile membrane), and miscellaneous substances (celluloid, Cellophane, rubber, olive oil, parchment, Gelfoam, fibrin film, Vinyon N, Orlon) have been used. The aim was to find a substitute that would simulate the properties of autogenous dura mater, but no one of these materials has fulfilled all the requisites.

The author obtained dura mater from homologous and heterologous species; it was sterilized chemically by immersion in ethylene oxide and preserved by freeze-drying. The prepared dura mater was implanted into surgically created dural defects in dogs and was compared with fresh autogenous dura mater as a replacement substance. Homologous sterilized, freeze-dried dura mater was found to be an effective dural graft, providing mechanical function while being invaded and replaced by the host. Inflammatory reaction and formation of adhesions were of the same order as those seen with fresh autogenous dural grafts. Heterologous sterilized, freeze-dried dura mater evoked a greater inflammatory response, but this was limited to the site of the graft and did not impair the function and integrity of the graft. It was concluded that homologous and heterologous ethylene oxide sterilized, freeze-dried dura mater can be used with confidence as a substitute for autogenous dura mater.

Dermatofibrosarcoma "Protuberans." O. Urteaga B. and A. Villanueva. Arch. peruanos pat. y. clín. 12:207-218 (no. 3 and 4) 1958 (In Spanish) [Lima, Peru].

Dermatofibrosarcoma protuberans is a benign, large-sized, molluscum growth with a tendency to local recurrence after it has been surgically removed. It can become malignant. When this happens, the tumor grows rapidly, gives multiple cutaneous, inguinal, visceral, and pulmonary metastases, causes progressive loss of weight, and follows an acute course with general symptoms of toxemia and cachexia. The histological picture of the primary and local recurrent tumors and of the metastases, removed during life of the patients or at autopsy, is that of a fibrosarcoma. The treatment consists of wide surgical removal of the tumor and the surrounding tissue and of grafting of skin tissue. The tumor is radioresistant. Irradiations are interdicted. They cause severe radiodermatitis and chronic necrotic ulceration.

The authors report 4 cases of dermatofibrosarcoma protuberans in men, between the ages of 31 and 58 years. The tumors developed from small nodules into nodular tumors, the diameters of which varied between 3 and 12 cm., they were located on the thigh, right arm, right axillary region, and left arm. In patients 1 and 4 the first tumor was removed surgically 8 months and 3 years, respectively, after its appearance. The tumor recurred within 7 months in one patient but did not recur in the other. In patients 2 and 3 the appearance of the tumor dated back 30 and 15 years respectively. The second patient had 2 recurrences before the tumor became malignant. The first recurrence occurred 30 years after surgical removal of the primary tumor. The malignant degeneration occurred 6 years after removal of the recurrent tumor and made amputation of the arm necessary. Six months after the amputation, abdominal and visceral metastases appeared. The patient died shortly after their appearance. No autopsy was made. The third patient had 2 recurrences after surgical removal of the first and recurrent tumors, during a 15-year period. Radiotherapy was given him, but it caused severe radiodermatitis and chronic necrotic ulceration which called for surgical removal of the damaged tissue and of the necrotic ulcer. The patient did not report for further observation. In none of the 4 patients did pulmonary metastases occur.

On the Treatment of Gastroduodenal Perforating Ulcer: Report on 184 Patients Operated on Between 1950 and 1958. A. Lupi. Riforma med. 73:205-213 (Feb. 21) 1959 (In Italian) [Naples].

The author reports on 184 patients, 176 (95.7%) male and 8 female, with gastroduodenal perforating ulcer, who were operated on at the surgery clinic of the University of Pavia, Italy, between November, 1950, and April, 1958. One hundred forty-six patients (79.3%) had duodenal ulcers, 37 (20.1%) had gastric ulcers, and 1 (0.6%) who had been subjected previously to suture and gastroenterostomy because of duodenal ulcer had a perforating jejunal ulcer. Sixty patients (32.63%) were 40 to 50 years of age; 43 (23.31%) were 50 to 60 years of age; 42 (22.82%) were 30 to 40 years of age; 25 (13.6%) were 20 to 30 years of age; 9 (4.9%) were 60 to 70 years of age; 4 (2.2%) were under 20 years of age, 2 being 19 years of age and the other 2 being 16 and 17 years of age, respectively; and 1 patient was 73 years of age. Resection was performed on 134 patients (73.4%), simple suture on 34 (17.9%), suture and gastroenterostomy on 15 (8.16%), and degastroenterostomy and resection on 1. Six patients (3.2%)—

4 with duodenal ulcer and 2 with gastric ulcer—died. Of the 146 patients with duodenal ulcer, 116 were subjected to resection and 2 died, 18 to simple suture and 2 died, and 12 to suture and gastroenterostomy and none died. General peritonitis was present in 7 of the 116 patients on whom resection was performed, in 1 of the 12 on whom suture and gastroenterostomy were performed, and in 9 of the 18 on whom simple suture was performed. Eight of the 37 patients with gastric ulcer presented diffuse peritonitis. Resection was performed on 18 of these 37 patients, simple suture on 16, and suture plus gastroenterostomy on 3. Two of these 37 patients died; one had been subjected to suture and the other to resection.

Emphasis is laid on early surgical intervention. Of 92 patients operated on within the first 6 hours after diagnosis, only 1 died, and diffuse peritonitis was never observed; of 78 patients operated on 6 to 12 hours after diagnosis, 2 died; and of 14 patients operated on 12 hours after diagnosis, 3 died. Comparison between patients of this series and the 126 patients with perforation who were observed in the same clinic in the 1940-1950 decade shows that diffuse peritonitis was a more frequent finding in the latter group due to a later surgical intervention. A finding that the author takes as an indication for resection, as preferable to suture, is that, of 56 patients on whom resection was performed 6 hours after perforation, only 2 died, while, of 25 patients on whom suture was performed 6 hours after perforation, 3 died.

The author lists the following factors as contraindications to resection: (1) if too long a period of time, usually more than 12 hours, has passed after the occurrence of perforation; (2) if the patient is over 60 years of age; (3) if the patient is not in good general condition because of circulation, liver, or kidney disease or chronic disease of the respiratory apparatus or because of obesity or alcoholism; and (4) if findings such as generalized peritonitis are present. The author believes that resection, with the exception of the above-listed instances, should be the operation of choice in patients with gastroduodenal perforating ulcers.

NEUROLOGY AND PSYCHIATRY

Anticoagulants for Occlusive Cerebrovascular Lesions. E. F. Vastola and A. Frugh. Neurology 9:143-148 (March) 1959 [Minneapolis].

Anticoagulants were administered to 41 men and 14 women (whose average age was 67.6 years) with a presumtive clinical diagnosis of a recent occlusive cerebrovascular lesion. None of the patients had more than slight hypertension, and in all of them a lumbar puncture before the institution of therapy did not reveal any evidence of hemorrhage. Practically all 55 patients first were given 200 mg. of Depo-Heparin Sodium intramuscularly, 50 mg. of heparin sodium intravenously, and 75 mg. of warfarin (Coumadin) orally. Warfarin was administered daily thereafter in doses sufficient to keep the prothrombin time at a value of 2 to 2½ times that of normal persons. With respect to progression of an incomplete neurological deficit, rate of recovery, and degree of recovery, the clinical course of these patients was not more favorable than that expected in a similar group treated only by supportive measures.

Twenty (36%) of the 55 patients had bleeding in various parts of the body during anticoagulant therapy; this high incidence is not believed to be related simply to the degree of prothrombin depression. It is highly probable that in 4 of these patients anticoagulation in the therapeutic range was responsible for extensive hemorrhage into the brain, with severe detriment to the patient's subsequent clinical course. In 3 of these patients hemorrhage occurred in the region involved by the initial occlusive lesion, and in the 4th the hemorrhage occupied a different region. The true incidence of this complication may safely be considered to have been higher, since in most patients an adequate search for it was not made. The risk of hemorrhage into the brain appears to contraindicate the use of anticoagulants in the treatment of cerebrovascular lesions under the conditions described in this report.

Diagnostic Considerations in Patients with Stroke. R. A. Kuhn. Geriatrics 14:135-149 (March) 1959 [Minneapolis].

The author calls attention to the ambiguity of the term "stroke." Hemiplegia usually accompanies such a condition, although paralysis of one side of the body is by no means essential to the picture. A variety of neurological symptoms and signs may be interpreted as being a stroke. In this paper, the author uses "major interference with brain function, customarily abrupt in onset" as a working definition of stroke.

Clinical examination may fail completely to differentiate a patient who later can be shown to have an occluded arteriosclerotic cerebral vessel from his clinically identical twin whose cerebrovascular tree is quite normal but who has an internal or common carotid artery mechanically plugged by a chronic intimal plaque and an organizing clot. Clinical neurological examination may fail even to differentiate supposed entities, such as "cerebral hemorrhage" and "cerebral thrombosis." It is unusual to be able to distinguish by clinical neurological examination alone such varied entities as rupture of a congenital cerebral aneurysm, leakage of an arteriovenous intracranial malformation, rupture of a cerebral vessel severely damaged by arteriosclerosis, sudden hemorrhage of a cerebral vessel invaded early by tumor, or so-called delayed intracerebral hemorrhage occurring several weeks after seemingly inconsequential head injury. Each of these lesions is capable of producing a hemorrhagic "stroke" clinically indistinguishable from that produced by the others. Each demands its singular therapy. In certain instances immediate treatment is imperative, and in others it may be wisest to temporize, but no therapeutic regimen can be followed with surety in the absence of an exact anatomic diagnosis.

The author presents and comments on the histories of 7 patients with "stroke" seen in consultation. In most of them a correct diagnosis was dependent upon the findings at arteriography. The advent of safe cerebral angiography has revolutionized the management of cerebrovascular disease by providing, in many instances, factual information in regard to the cause of the stroke. It is now clear that approximately one-third of all patients who have strokes suffer from cervical carotid artery disease. In many instances, these arterial occlusions are surgically remediable, the surgical treatment resulting in increased blood flow to the brain. Cerebral angiography should be considered a vital and routine part of management of all patients with hemiplegia or other manifestations of stroke with or without intracranial bleeding.

The Stiff-Man Syndrome. D. Brage. Rev. clín. españ. 72:30-38 (Jan. 15) 1959 (In Spanish) [Madrid].

The stiff-man syndrome was described for the first time in the American literature 30 years ago. Fourteen cases have been reported. The syndrome consists of progressive, generalized, acute, painful muscular spasm and muscular rigidity which start at the neck and symmetrically in the legs. Involvement of the rest of the muscles depends on the acute, hyperacute, or subacute form of the disease. The disease is of unknown etiology. Heredity, neurological diseases, or metabolic disorders have not been found to be causal factors. Roentgen-ray examination of the spine shows spondyloarthrosis. The cerebrospinal fluid is normal, and the mental condition of the patient is normal. There are no clues for a diagnosis until the whole syndrome develops. The abdominal muscles become as hard as though made of wood, and cramps and painful spasms are frequent. The patient is forced to lie in bed in the dorsal position. If he is placed in a standing position, he falls down as if he were a "wooden man." No treatment is available. The brain was studied in one autopsy reported in the literature; it was found to be normal.

The subjects of this report were 2 men, 52 and 71 years old, in whom the disease started 5 and 20 years, respectively, before consultation. The syndrome was typical. Muscular rigidity was complete within 2 years from appearance of the first symptoms in the first patient and within 10 years in the second. Both patients had normal mentality. Both had spondyloarthrosis and hallux valgus. Rigidity involved all the muscles, including those of the face, hands, and feet. Blood and cerebrospinal fluid findings were normal. Cortisone and drugs of the curare type were of no effect. One of the patients was discharged from the hospital at his own request; he did not reappear for observation. The other patient received treatment with bis (4,6-diethylamino-1, 3, 5-triazin-2-yl) hydrazine dihydrochloride (Ciba 13,155) in daily doses of 800 mg. This treatment caused a slight improvement of muscular rigidity and spasm, and the patient was able to walk, although with some difficulty. The duration of treatment in this second case is not specified by the author.

Levomepromazine in Psychiatry. L. Telatin. Minerva med. 50:166-169 (Jan. 24) 1959 (In Italian) [Turin, Italy].

The author reports on the effect of Levomepromazine, a new phenothiazine derivative, on a group of psychiatric patients. Patients with melancholia received an average dose of 150 mg. per day; the initial dose was 50 mg. per day, and in a short time it was increased to 150 to 200 mg. per day. The dose in patients with schizophrenic syndromes or chronic psychosis was increased very early to 150 mg. per day. The patients were kept under close observation, and if it appeared that the drug had little or no effect, the dose was increased by 25 mg. per day up to a high of 300 to 400 mg. per day. This maximal dose was continued for one month or more; then it was gradually reduced to a maintenance dose of 25 to 50 mg. per day in patients with melancholia and to 100 to 150 mg. per day in patients with schizophrenic syndromes. The maintenance dose was given for long periods of time to avoid relapses. The patients were kept in bed during the first few days of treatment so that there would be no collapse resulting from the hypotensive effect of the drug.

Levomepromazine had an hypnotic effect on all the patients; on the average, the morning and afternoon doses induced sleep for 2 or 3 hours, and the evening dose was followed by sound sleep the entire night. The sleep induced with Levomepromazine was not disturbed (as frequently happens with chlorpromazine or reserpine) by painful dreams or nightmares. The drug did not cause any disturbances or unpleasant sensations. A rapid improvement in behavior, decreased agitation, and a return of logical speech were observed in patients with schizophrenic syndromes. This improvement lasted for a short time only in some patients, a little longer in others, and was still present some months after the beginning of treatment in others. Complete remission of the symptoms was obtained in one patient who had suffered chronic hallucinotic psychosis for 3 years and had derived no benefit from previous treatments. A good result was also obtained in one patient with obsessive psychoneurosis, and improvement was noted in a patient with chronic schizophrenic excitation. Very good results or complete failures were observed in patients with depressive anxiety.

The good effect of Levomepromazine in patients who benefited from the drug became manifest early. When there was no sign of improvement during the first 15 days of treatment, the patients usually failed to derive any benefit from the drug. The treatment might be reinstituted after a 20-to-30-day rest, and occasionally good results followed in some patients. Levomepromazine had a good effect on the general condition of the patients, causing an improvement in appetite and being well tolerated. It had no toxic effect. Various laboratory tests always gave negative results.

Enuresis in Adults: Preliminary Study. E. Y. Williams. M. Ann. District of Columbia 28:125-128 (March) 1959 [Washington, D. C.].

The effects of nocturnal enuresis on grown-ups has been studied in 16 patients, their ages ranging from 19 to 41 years. Of the 16 patients, the parents of 7 were also bed wetters. It was observed that this condition had definitely affected the patients, not only as to their personality make-up but also as to their outlook on life, and thus had crushed their possibilities for greater success. The educational aspects were probably one of the most important factors noted. Three of the 16 patients wanted to be lawyers, 1 a physician, 1 a dentist, 1 a social worker, 1 a teacher, 1 a policeman or a fireman, and 3 wanted to be engineers; 5 patients had no definite goal. Eight of the 16 patients were good students and could have gone to college; 4 had scholarships, but all of them refused because of the problem anticipated in dormitories. Two patients did not even finish high school, because they believed that other children were moving away from them due to odor of urine. Only 2 of the 16 patients married, and they were not able to make adequate marital adjustments. The male patients were very shy in their relationship with girls, and they lacked the male aggressiveness. Predisposing causes, such as highly acid urine, cystitis, preputial adhesions, vesical calculus, and irritation from pinworms, were ruled out by history and examination in these 16 patients. All the patients were deep sleepers, and bladder awareness was noted to be absent. Depth of sleep was considered of great importance. It seemed that drugs which lessened the depth of sleep had a better chance of decreasing nocturnal enuresis than did sedatives. At present 6 of the 16 patients have been successfully treated with a drug designed to lessen depth of sleep, and although some supportive psychotherapy was carried out, the results have been most convincing as well as gratifying.

GYNECOLOGY & OBSTETRICS

Resuscitation of Stillborn Infants. H. H. Epple and J. M. Sutherland. Obst. & Gynec. 13:259-263 (March) 1959 [New York].

A 30-year-old gravida at 39 weeks' gestation was admitted in labor to the obstetric service of the Cincinnati General Hospital. Five hours later she began to crown, and nitrous oxide–oxygen anesthesia was given. The fetal head emerged spontaneously after a mediolateral episiotomy. Further delivery was prevented by shoulder dystocia. After fruitless efforts resulting in a delay of 11 minutes, the posterior arm was extracted, and simultaneously the posterior shoulder was rotated to the anterior position. At this time the head was cyanotic, and no fetal heart tones were heard on auscultation of the accessible left chest. Delivery was completed in 3 more minutes with the birth of a female infant weighing 5,900 Gm. (13 lb.). Immediate examination of the infant revealed no respiratory effort or heart beat. Because the heart tones were still not heard 3 minutes after delivery, the chest was opened through the left 5th intercostal space. The heart was flabby and dilated. The pericardium was not opened. Three minutes after delivery, 6 minutes after fetal heart beat was known to have disappeared, and 14 minutes after arrest of the shoulder, cardiac massage was started by rhythmic squeezing of the heart with the forefinger against the sternum from base to apex. The myocardium quickly regained its tone, and soon thereafter the first slow and irregular contractions were felt. A normal sinus rhythm of about 120 beats per minute followed after 3 minutes of rhythmic digital compression. This rhythm continued without further abnormality. A first poor cry was heard 15 to 20 minutes after extubation. After the 20th day the infant improved considerably. At one month of age the child was smiling and was discharged with no detectable abnormalities. At 4 months her motor and adaptive behavior was judged normal or even precocious, though it is impossible to give a definite prognosis at that age.

The successful resuscitation of this stillborn infant prompted the authors to review perinatal deaths among 4,200 deliveries which occurred in 1957 at the Cincinnati General Hospital in order to determine possible candidates for cardiac resuscitation. There were 11 fetuses among the 4,200 deliveries which were alive on admission of the mother to the hospital and which died in the one hour before delivery. [The surviving stillborn infant reported here is included among the 11 fetuses.] Two of the 11 fetuses had histological evidence of overwhelming intrauterine infection which could have accounted for death. There were histories of progressive intrauterine distress starting 1½ to 3 hours before delivery in 4 other fetuses, of whom 2 were born of bleeding mothers, 1 was born with a nuchal cord, and 1 was delivered after prolapse of the cord. Of the remaining 5 fetuses, 1 was a 1,600-Gm. (3½-lb.) first twin, 1 was born of a febrile mother with a diagnosis of pneumonia, and the other 3 (including the subject of this report) were delivered after shoulder arrest. In one of the 3 fetuses with shoulder arrest, there was a 5-minute delay between delivery of the head and of the shoulders; in another there was a 12-minute delay, pulsation having been absent 9 minutes before the delivery of the shoulders. Thus, there were 3 definite candidates and 2 questionable candidates for cardiac resuscitation among the 4,200 deliveries.

Cardiac resuscitation seems warranted in infants who have had sudden cardiac arrest from any cause and who probably have a more or less intact brain, as in infants born after a shoulder arrest or in infants in whom the period of anoxia is well defined and of short duration. Therefore, cardiac resuscitation should be tried in selected instances with a clear understanding of the possibilities for success. The airway must be cleared and preparation made for oxygenation before the chest is opened. Electrical treatment is used in ventricular fibrillation; this form of cardiac arrest has not been observed in newborn infants. Therefore, resuscitation of stillborn infants is best accomplished by restoration of the respiratory system and simultaneous rhythmical manual compression of the heart.

Management of Ovarian Carcinoma in 123 Patients: With Particular Emphasis on the Prophylactic Use of Radioactive Gold. J. C. Weed and D. F. Barraza. South. M. J. 52:278-282 (March) 1959 [Birmingham, Ala.].

The authors review observations on 123 women with malignant ovarian tumors, who were admitted to the Ochsner Clinic in New Orleans for diagnosis and therapy between 1942 and 1958. The youngest patient was 25 years of age, and the oldest 82 years. Seventy-two of the 123 women were between 40 and 60 years of age. About one-third of the patients were childless. Eight of the 123 patients were asymptomatic. Symptoms of the other patients included pelvic pain, abdominal swelling, backache, pelvic pressure, and vaginal bleeding. For cases not detected early in their course, survival rates were poor. All patients (32.5% of the total) whose primary tumor was inoperable, or incompletely removed, failed to survive more than one year in spite of surgical and adjunctive therapies. Nitrogen mustard, deep roentgen irradiation, and radiogold (Au^{198}) were the adjunctive methods used.

The authors first used Au^{198} intraperitoneally in 1952 as an adjunct to surgical and roentgen-ray therapy for carcinoma of the ovary. From 5 to 9 days postoperatively, between 125 and 150 mc. of Au^{198} was instilled into the peritoneal cavity with 500 cc. of isotonic sodium chloride solution; 26 patients with ovarian cancer were treated in this way. In 20 of these, treatment was directed toward preventing metastasis, and in 6 it was given in an effort to prevent reaccumulation of ascitic fluid. Undesirable effects of administration of Au^{198} were minimal. In patients with ascites, few untoward reactions were noted. In only one patient did ileus develop, and this was of moderate intensity. Isolation of the patient because of radioactivity was more troublesome than local reactions.

The efficiency of Au^{198} in reducing the necessity for paracentesis for ovarian carcinomatosis was difficult to assess. Rapidly progressive tumors were little affected, but in slowly progressive tumors accumulation of fluid was well controlled. The authors employed intraperitoneal administration of Au^{198} prophylactically in patients in whom surgical cure was thought possible. Gross metastatic spread is regarded as a contraindication to use of this agent.

Use of intraperitoneal implantation of Au^{198} does not contraindicate the use of deep roentgen-ray or radio cobalt (Co^{60}) therapy later. In one patient in whom Au^{198} was instilled postoperatively, residual localized tumor was discovered after 8 months. Deep therapy with Co^{60} was administered elsewhere to the area of recurrence. Exploratory laparotomy 3 years postoperatively revealed no malignant lesion, and the patient has survived 2 additional years without recurrence. Au^{198} should be administered intraperitoneally in those patients whose ovarian carcinoma is ruptured during removal, in those who have ascites but no obvious metastasis, or in those whose tumor shows evidence of break through the surface. Supplemental roentgenotherapy may be directed later to isolated metastatic lesions.

Endometriosis of a Hernia Sac. I. H. Dreishpoon and E. Klempner. New York J. Med. 59:847-850 (March 1) 1959 [New York].

A 38-year-old woman with endometriosis in a femoral hernial sac and a 45-year-old woman with endometriosis in an inguinal hernial sac were operated on in the department of obstetrics and gynecology of the Mount Sinai Hospital in New York. The finding of ectopic endometrial tissue in the wall of the femoral hernia in the first patient was an accident, since there was no clinical evidence of pelvic endometriosis, nor was there any gross evidence of endometriosis at the site of the hernia. In addition, the patient denied any cyclic exacerbations or remissions in her asymptomatic hernia. In the second patient, there was evidence of endometriosis in the groin surrounding the hernia, making the surgical procedure a difficult one, although clinically there were no signs of pelvic endometriosis. This patient also denied having any cyclic variation in her asymptomatic inguinal hernia, which was erroneously diagnosed as a neoplasm probably arising from the pubic bone.

The diagnosis of femoral or inguinal endometriosis can be extremely difficult preoperatively. The addition of a hernia in these locations can make the diagnosis more difficult. With a history of cyclic exacerbations of symptoms, such as pain, tenderness, and swelling at the time of menstruation, the diagnosis becomes simple. The diagnosis becomes even more certain if clinical signs of endometriosis are present in the pelvis. At operation for a suspected endometrioma of the inguinal or femoral region, care must be taken not to overlook the presence of an associated and intimately adherent hernia. Endometriosis of a hernia sac could be best explained by direct implantation to the peritoneum of the sac after regurgitation from the tubes, but this concept, proposed by Sampson for endometriosis of the hernia sac, was untenable in these 2 patients because of the clinical lack of evidence of pelvic endometriosis in both cases. Therefore, Javert's theory of lymphatic metastasis to adjacent organs appeared more feasible in these patients.

INDUSTRIAL MEDICINE

Siderosis: Additional Observations Over a Period of Eight Years on Sixty-nine Foundry Cleaning Room Employees. L. E. Hamlin. J. Occup. Med. 1:79-93 (Feb.) 1959 [Chicago].

In April, 1950, the results of a study of 69 workers who had been exposed to foundry cleaning room dust for long periods of time were published by Hamlin (the author of this report) and Webster. Roentgenograms of the chests of these foundry workers disclosed pulmonary nodular shadows compatible with siderosis, but other investigations revealed no clinical signs or symptoms that might suggest impairment of the lungs. Industrial hygiene surveys of the working environment demonstrated exposure to dust containing high atmospheric concentrations of iron oxide and low amounts of free crystalline silica along with other constituents. This paper presents the results of follow-up clinical and roentgenologic studies on the foundry cleaning room employees after a period of 8 years' further observation.

Allowing for 5 deaths from causes unrelated to occupation and 5 terminations of employment, 85.5% of the workmen in this group are living, and 69.5% are actively employed, the majority at their regular jobs of grinding castings. No progression of the nodular shadows previously noted is apparent in serial chest roentgenograms of these workers, despite the fact that at least half of them have continued to work under fairly high atmospheric concentrations of cleaning room dust over a long period of time. No adequate reason has been demonstrated to alter the conclusion reached in the original study that the nodular patterns observed in these employees' chest roentgenograms represent mainly siderosis rather than silicosis. The present study again demonstrates the necessity for adequate physical examinations, including detailed occupational histories and knowledge of atmospheric concentrations of harmful dust, before making a diagnosis of specific pneumoconiosis.

Incidence of Human Anthrax in North Kanara. N. S. Deshpande. J. Indian M. A. 32:13-14 (Jan. 1) 1959 [Calcutta].

An outbreak of human anthrax in Supa, a village in the North Kanara district in Mysore state, was preceded by an anthrax epizootic among the animal population, including cattle and forest animals. All 5 patients with anthrax treated in the Supa dispensary had the cutaneous form, but owing to a lack of laboratory aids, cases of pneumonic and intestinal anthrax may have been missed. The Tabanus fly, a large blood-sucking fly, is believed to act as carrier of anthrax from animals to man, the blood in the stomach of one such fly having been found to contain anthrax bacilli. The 5 patients were agriculturists whose cattle had died of anthrax; 3 of these patients gave a history of being bitten by a Tabanus fly.

The umbilicated lesion was surrounded by a zone of induration, and there was itching and swelling of the affected part. In 4 of the 5 patients pneumonia developed, and in 2 the central nervous system became involved, as evidenced by a semiconscious state. Penicillin in large doses proved to be the drug of choice. In patients with severe toxemia, 2,800,000 units of penicillin divided into 2 doses was administered daily until the toxemia and fever subsided. This required 2 or 3 days, the fever subsiding by lysis. Subsequently 400,000 units of procaine penicillin was injected twice daily until the eruption was covered with a scab and the swelling had completely disappeared. This took about 8 to 10 days. The complete healing of the eruption was slow.

Anuria Caused by Carbon Tetrachloride Intoxication (On the Basis of 25 Observations). G. Richet, J. Crosnier and J. Lissac. Rev. prat. 9:591-610 (Feb. 21) 1959 (In French) [Paris].

Twenty-five patients with anuria caused by the inhalation of carbon tetrachloride during their work were observed within 4 years at the Hospital Necker, Paris. Carbon tetrachloride is at the present time mainly responsible for acute renal insufficiency of toxic origin. The toxicity of the manipulated substance is almost always ignored. This fact, in addition to the absence of morbid manifestations at the time of inhalation of the poisonous agent, and the quiescent period of 3 days before the onset of anuria explain why the disease was recognized in only 2 of the 25 patients before their admission to the specialized service. Digestive disturbances, vomiting, constipation or diarrhea, pulmonary manifestations, fever, dysphagia, subicterus, hemorrhagic syndrome, and mild hypertension are the signs preceding or attending the inception of anuria precipitated by carbon tetrachloride. Although these symptoms are specific of this type of acute renal insufficiency, they contribute toward surprising diagnostic errors. The principal obstacles preventing a spontaneous cure are paroxysmal vascular accident, acute pulmonary edema, or cerebral edema. These complications are favored by the direct action of the toxic vapors on the capillary system, and, besides, these can also be elicited by a moderate water-salt overload. It is, therefore, imperative to impose extreme water restriction on these patients and to forbid the administration of sodium as long as anuria persists.

If a cure has been obtained, it is usually complete insofar as one may judge from the findings of the clinical and biological exploration in this series. It was possible to demonstrate that the renal clearance of mannitol and of *p*-aminohippuric acid returned to normal in 9 patients. The frequent intoxications caused by carbon tetrachloride and the fact that it represents a grave occupational hazard suggest that public authorities take measures to limit its use and that it be replaced by less toxic compounds as a solvent and dry cleaner.

Rehabilitation of the Flyer Following Thoracotomy. F. E. Foley, S. H. Bear, J. A. Jarman and others. J. Aviation Med. 30:113-117 (Feb.) 1959 [St. Paul].

Twenty-nine major thoracic surgical procedures were performed, during the 4-year period from 1954 to 1958, on 27 patients who reported from flying status to the U. S. Air Force Hospital, Maxwell Air Force Base, Alabama. Two patients each underwent 2 thoracic operations. The first patient had bilateral apical wedge resections and bilateral pleurodesis for localized apical bullae, accomplished in 2 stages by anterior thoracotomies 3 weeks apart. The second patient underwent right pneumonectomy for a peculiar organizing and calcified pneumonitis, followed by a subcostal, extraperiosteal, Polystan (a polyethylene plastic) plombage to prevent mediastinal shift and overdistention of the contralateral lung. Three patients underwent resection amounting to a lobectomy or more. The remainder of the pulmonary resections were single or multiple wedge resections. Seven of the wedge resections were for localized bullous emphysema and recurrent spontaneous pneumothorax. Six wedge resections were performed for chronic infectious processes. A wedge and a local resection were performed on 2 patients with congenital pulmonary disease. Resection of chest wall tumors was carried out in 2 patients, one of whom had an eosinophilic granuloma with cortical invasion and spontaneous fracture of the left third rib. A neurofibroma of the intercostal nerve was found in the second patient and was resected. Hiatus hernias in 3 patients and a traumatic diaphragmatic hernia in 1 patient were successfully repaired. One patient was treated for a shotgun wound of the chest.

One of the 27 patients died in an accident during convalescence. Two patients were grounded permanently for pulmonary insufficiency, but both returned to military duty; in each instance the patient was incapacitated for flying by his preoperative condition alone. One patient was grounded because of a relatively recent operation. The remaining 23 patients were restored to flying duty by 24 major operations.

PATHOLOGY

Clinical Syndromes Associated with Deficient Lung Fibrinolytic Activity: I. A New Concept of Hyaline-Membrane Disease. J. Lieberman. New England J. Med. 260:619-626 (March 26) 1959 [Boston].

In an attempt to confirm the concept that a defect in lung fibrinolytic enzyme activity may be an underlying factor in the pathogenesis of pulmonary hyaline-membrane formation, the author studied the tissue fibrinolytic activity in lung and several other organs of 49 fetuses and infants who were either stillborn or died in the neonatal period and on whom autopsies were performed. In 8 of the infants who died 6 to 48 hours after birth, pulmonary hyaline-membrane formation was found at autopsy. The tissue activator of plasminogen was found to appear in lung as early as the third month of gestation, 33 of the 41 fetuses and infants without pulmonary hyaline-membrane formation showing this activity. None of the 8 infants with hyaline membranes showed this activity. A preliminary review of reproductive histories of mothers who were delivered of infants with confirmed hyaline-membrane formation showed a tendency to multiple neonatal deaths suggestive of hyaline-membrane disease.

Previous reports by other workers have shown that hyaline-like membranes can be produced easily by oxygen poisoning in guinea pigs and rabbits, but not in rats. Experiments performed by the author on guinea pigs showed that hyaline-membrane formation appeared much more readily when oxygen poisoning was supplemented by nebulized filtered amniotic fluid. Plasminogen-activator activity was studied in the lung tissue obtained from rats, guinea pigs, and rabbits. The lungs of rabbits and guinea pigs were found to be totally deficient in this activity, whereas the enzyme was readily demonstrable in the lungs of rats.

The reported data suggest that a predisposing factor in hyaline-membrane formation of the newborn infant is the absence of plasminogen-activator activity in lung. An interaction between amniotic fluid or tissue thromboplastin and other clotting factors in an alveolar effusion results in deposits of fibrin that are transformed into "hyaline membrane" postnatally. Such fibrin deposits would be lysed normally through action of the fibrinolytic system if the tissue activator were present. The defect does not appear to be related necessarily to the degree of prematurity but may represent a genetic aberration.

Diffuse Progressive Interstitial Fibrosis of the Lungs. K. A. Larsen. Acta path. et microbiol. scandinav. 45:167-185 (no. 2) 1959 (In English) [Copenhagen].

Larsen points out that diffuse progressive interstitial fibrosis of the lungs was first described as a distinct entity in 1934 and 1944 by Hamman and Rich, and that since then several other reports have appeared which show that this disease is a well-defined condition either not previously known or perhaps hidden under other diagnoses. About 30 cases have been published, and the condition has become known as the Hamman-Rich syndrome. While many of the reported cases were relatively acute, extending over a period of a few weeks or months, there have also been several cases extending over a period of years. The clinical and pathological findings suggest that all these cases constitute an entity with the same etiological factors. However, there have also been reports of cases of progressive dyspnea, characterized by cyanosis and certain other pathological findings but designated as "honeycomb lung," "interstitial pneumonitis," "pulmonary muscular hyperplasia," "diffuse cystic lungs of granulomatous origin," or "diffuse myomatosis and cyst formation in the lung." Several of these cases seem, both clinically and pathologically, to be similar to the diffuse progressive interstitial fibrosis of the lungs described by Hamman and Rich.

The author says that in the pathology laboratory at Ulleval Hospital in Oslo over a period of about 3 years 5 cases were observed which resembled or were identical with the Hamman-Rich syndrome. The histories of these 5 patients are presented; in most of them the syndrome was of relatively long duration. All the patients died and were subjected to autopsy. The main symptoms were progressive dyspnea, cough, and, later, cyanosis. Some patients had clubbing of the fingers and watch-glass nails; in the later stages they had signs of failure of the right ventricle. Roentgenologically there were progressively increasing numbers of small opacities in both lungs, some miliary and some forming a network. In other areas the opacities were more diffuse with small cystic translucencies often close together. Pathologically the lungs were firm, sometimes rubbery. Microscopic studies revealed disappearance of respiratory epithelium and compact fibrosis with marked development of reticulin fibrils. Small cystic spaces lined with epithelium similar to that in bronchioles were also observed.

Observations by the author pointed to a respiratory virus infection as the primary process. Three of the patients had an introductory acute febrile respiratory infection which was suspected of being virus pneumonia, and in one patient such an infection led to death in 5 weeks. In most patients the respiratory symptoms and roentgenologic opacities progressively increased after the acute respiratory infection. It is considered highly probable that the primary process was a virus infection affecting the bronchioles and more distal air spaces, and that this was followed by relatively extensive epithelial necrosis and sometimes also necrosis of the interstitial mesenchymal tissue in the same areas. Such extensive necrosis may lead to collapse of the reticular framework in the alveolar walls, making orderly regeneration of the lung lobules with the respiratory elements impossible. Cystic spaces form between the collapsed areas, and these will be lined with epithelium from the remaining bronchioles or small bronchi. Interstitially there will be proliferation of the mesenchymal tissue and formation of numerous reticulin fibrils. The author feels that these processes explain the picture seen in the patients presented. Complete cirrhosis of the lung, like virus hepatitis, may lead to cirrhosis of the liver.

Mucormycotic Infection of Arteriosclerotic Thrombus of the Abdominal Aorta: Report of a Case. R. Fienberg and T. S. Risley. New England J. Med. 260:626-629 (March 26) 1959 [Boston].

The authors report a 45-year-old woman with controlled diabetes mellitus, in whom infection caused by a fungus of the genus Mucor was limited to the abdominal aorta. The patient was admitted to the Beverly (Mass.) Hospital 2 weeks after the onset of pain in the lower abdomen and was found to have a large abscess in the right lower quadrant extending in the pouch of Douglas. She was treated conservatively with bed rest and administration of 250 mg. of chloramphenicol 4 times daily; the abscess gradually subsided without surgical drainage, and she was discharged after 2 weeks. Two months after the onset of the previous symptoms, the patient was readmitted to the hospital for an elective interval appendectomy. At operation, an old perforation of the appendix was found, the tip of the appendix being embedded in a small abscess cavity less than 2.5 cm. in diameter. A culture of the contents of this abscess yielded anaerobic streptococci. Microscopic examination of the operative specimen revealed perforation of the appendix, with a foreign body reaction around extruded fecal material. Postoperative distention was treated by gastric suction. Tetracycline was given after the operation. On the third postoperative day the patient's temperature rose to 104 F (40 C), and she died on the 5th postoperative day with high fever and shock. Autopsy was performed and revealed an occluding thrombus of the abdominal aorta just above the bifurcation, being attached to the intimal surface. Within the thrombus, the intima, and the remnants of the media, nonseptate (coenocytic) hyphae varying greatly in width were seen. Mycelia of the mucormycotic fungus thus were seen in the thrombus near its attachment to the wall of the aorta and in the wall itself.

It is postulated that mycethemia followed the interval appendectomy and led to infection of a mural thrombus previously formed at the site of an arteriosclerotic plaque in the abdominal aorta. Complete occlusion of the lumen of the abdominal aorta was the result of the fungal infection. The antibiotic administered after the interval appendectomy was considered to be an important factor in facilitating the invasion by the fungus. No other report has been found in the literature dealing with the invasion of the abdominal aorta by the fungi of mucormycosis. The importance of mucormycosis as a complication of such disorders as diabetes mellitus, leukemia, multiple myeloma, fatal burns, and cirrhosis has been stressed.

Do Smoked Foods Have a Carcinogenic Effect? N. Dungal. Krebsarzt 14:22-24 (no. 1) 1959 (In German) [Vienna].

Smoked meats and fish constitute an important food element for the population of Iceland. Since cancer of the stomach is rather frequent in Iceland, accounting for about half of all cancers in men, the author investigated whether smoked foods might represent a danger in this respect. He first carried out feeding experiments on rats. Most of the rats fed exclusively with smoked meat died within a short time; so subsequently the rats were given daily only 20 Gm. of smoked meat together with a standard diet. Two of 4 rats, which originally had been fed with smoked meat, died after 18 months; one was found to have cancer of the liver with peritoneal metastases, and the other had a malignant tumor of the lung.

Smoked meats, particularly mutton, and several types of smoked fish were examined for their aromatic hydrocarbon content with the aid of chromatographic analysis. While some of the hydrocarbons found in considerable quantities are not carcinogenic by themselves, they might act as cocarcinogenic substances. Considerable amounts of the highly carcinogenic polycyclic hydrocarbon, benzpyrene, were also detected in the smoked foods. Although smoked foods may not be the main cause of gastric cancer among Icelanders, the author warns against prolonged smoking of foods. He believes that foods smoked only briefly are probably not dangerous, but foods smoked for weeks or months, as is frequently the case with lamb and mutton in Iceland, may contain carcinogenic substances in sufficient quantities to make them dangerous.

Congenital Virilizing Adrenal Hyperplasia in Identical Twins. N. G. Schneeberg, A. Steinberg, M. M. Malen and others. J. Clin. Endocrinol. 19:203-212 (Feb.) 1959 [Springfield, Ill.].

The twins presented had been born in January, 1948, at the southern division of the Albert Einstein Medical Center in Philadelphia after an uncomplicated full-term pregnancy. The family physician noted enlargement of the clitoris in both babies, but, despite his suggestions, further studies were not pursued. At the age of 3 years the clitoral enlargement had increased. A few pubic hairs appeared at age 4. Marked acceleration of growth occurred between the 5th and 6th years. Axillary and pubic hair and hirsutism of the arms, legs, upper lip, and chin became well marked. There was a progressive increase in virilization and the appearance of facial acne during the 6th and 7th years.

The twins were hospitalized in June, 1955, when they were 7½ years of age. They were tall, alert, intelligent children whose appearance resembled that of somewhat muscular 12-year-old girls. Their voices were low-pitched, and there were multiple small acneform lesions and moderate oiliness of the skin of the face. Soft downy hair grew on the upper lips, and sideburns were prominent. Axillary and pubic hair was of the adult female type, and the axillas contained an adult quantity of sebaceous secretion. There were a few fine colorless striae over the upper anterior thighs. In each child the clitoris was markedly enlarged. There was a glans-like cuff at the distal portion of the clitoris. The vaginal introitus and urethra were separate and in normal relationships. Vaginal dilation with a nasal speculum revealed a tiny cervix in each twin. The diagnosis of congenital virilizing adrenal hyperplasia was based on hypertrophy of the clitoris at birth, progressive virilization and accelerated growth, elevated urinary values of 17-ketosteroids and pregnanetriol, and female sex chromatin pattern.

Corticosteroid therapy was begun in June, 1955. Considerable difficulty was encountered initially. Therapeutic trials with intramuscular injections of a long-acting hydrocortisone preparation and the oral administration of prednisone, fluorohydrocortisone, and methylprednisolone did not consistently suppress adrenal androgen production but (except for methylprednisolone) did induce Cushingoid phenomena. Finally, a successful regimen was achieved; either 25 mg. of cortisone or 8 mg. of prednisone was injected intramuscularly every other day. This suppressed adrenal hyperfunction without producing side-effects. The occurrence of congenital virilizing adrenal hyperplasia in identical twins lends support to the concept of a genetic origin. The rarity of this syndrome in identical twins is not surprising.

Morphologic Characteristics of the So-called Intra-articular Free Bodies. S. Di Filippo and R. Ziaco. Policlinico (sez. prat.) 66:181-186 (Feb. 9) 1959 (In Italian) [Rome].

The authors report on a morphologic study of 27 intra-articular free bodies removed surgically from 16 subjects, 12 male and 4 female; more than 1 free body was removed in 5 patients. The patients ranged in age from 19 to 47 years; 10 of them were between 22 and 35 years. Trauma of the articulation occurred in 13 patients; nothing is known of the etiology of the free body in the other 3. The free body had been present for from 7 to 15 days in 2 of the 16 patients, for from 16 to 30 days in 4, for from 1 to 3 months in 3, for from 4 months to 1 year in 4, for from 2 to 4 years in 2, and for more than 5 years in 1. All the patients suffered pain on movement of the articulation involved; in some patients the joint presented some swelling. Thirteen of the intra-articular free bodies removed consisted mainly of cartilaginous tissue, 7 of cartilaginous and bone tissue, and 6 of fibrous connective tissue, fibrous cartilaginous tissue, or fragments of altered synovial membrane. Intra-articular free bodies were found to be the result either of lesions of articular tissue which had undergone no alterations up to the formation of the free body or of primitive alterations of the articular tissue with consequent detachment of a part of this altered tissue. In simple traumatic alterations, such as mechanical detachment of a part from the articular tissue, the structure of the intra-articular free body corresponds completely to that of the tissue from which the free body had become detached. When the detachment of the free body was preceded by arthrosis or arthritis, the free body showed signs of dystrophy and at times of necrobiosis. The authors believe that under favorable biological condition, as that afforded by synovial fluid present in the lumen of an articulation, the bone tissue and the cartilaginous tissue retain their vital capacity and their vital activity as well. The latter consists in the division and reproduction of cells and in their capacity to undergo changes and metaplastic modifications.

Pilonidal Sinus of the Axilla. E. S. J. King. Australian & New Zealand J. Surg. 28:196-201 (Feb.) 1959 [Melbourne].

The author points out that the term "pilonidal sinus" has been applied most commonly to the condition found in the sacrococcygeal region, but its rare occurrence in other parts of the body is significant because of the light it sheds on the pathogenesis. The word "pilonidal" means merely "nest of hair" and has no topographic or etiological connotation. The author cites literature reports on various unusual locations, such as in the perianal region, above the symphysis pubis, in the hair-bearing area of the face and neck, and in the interdigital regions.

The author presents the history of a 56-year-old woman with a painful area in the left axilla over the previous 8 weeks. It had been red and hard but had improved gradually without special attention. On examination, a small indurated area in a crease just behind the anterior axillary fold and measuring about 2.5 cm. in diameter was observed. A few hairs were noticed protruding from a small sinus in the middle of the area. The patient agreed to its removal. The macroscopic and microscopic aspects of the surgical specimen are described and discussed. The site of the sinus in a sulcus just beneath the anterior axillary fold supports the general suction hypothesis. A hair or sharp body could penetrate the normal skin, or a hair follicle or sweat gland may be the point at which some material may enter from without. Once the opening is formed (or a natural space entered), the foreign body or bodies will facilitate infection and enlargement of the opening.

There has been considerable discussion about the orientation of hairs in the sinus. It is not necessary to depend on this feature to demonstrate that material is actually sucked into the sinus. In the present case the talc granuloma at the fundus of the sinus is further indication of the mode of development of, and external origin of material in, the sinus. Talc powder had been used, and the distribution of the material and cellular reaction indicate that considerable material had entered the area.

RADIOLOGY

Radiological Manifestations of Tuberose Sclerosis. P. H. Whitaker. Brit. J. Radiol. 32:152-156 (March) 1959 [London].

Tuberous sclerosis is also known as Bourneville's disease, because it was first described by him in 1880. It is a rare disorder in which tumors and sclerotic patches appear in the cerebrum and are associated, in some cases, with manifestations in other organs and in the skin. More recently lesions have been recorded in the skeleton. Clinically the association of epilepsy, mental retardation, and the cutaneous manifestations are characteristic. The association of skeletal defects may not be recognized unless they are specifically sought. This report is concerned with skeletal changes which were found in 3 patients. The first patient was a 17-year-old epileptic boy of subnormal mentality, who had typical facial adenomas, one subungual fibroma, and scattered pigmentation of the trunk. Calcifications existed in the brain, and the bones of the skull had a mottled appearance. The second patient was a 9-year-old ament who had extensive sebaceous adenomas of the face and back. Subungual fibromas were present on the hands and feet, and he was deaf and had retinal disturbances. The only skeletal manifestations were changes in one rib, resembling a fibrous dysplasia. The third patient was a woman of 37 years, who was an epileptic of subnormal mentality but capable of earning her living in domestic employment. She showed facial adenomas with nail-bed fibromas of the hands and feet; also generalized changes throughout the skeleton and pulmonary changes.

The author points out that roentgenologic studies may help in the diagnosis of tuberous sclerosis by demonstrating visceral adenomas, particularly in the kidney, the large intestine, and the duodenum, and cystic changes in the lungs. Defects in the liver and cardiac muscle are less likely to be roentgenologically demonstrated, except as alterations of outline. Cerebral changes appear roentgenologically as calcifications in areas of gliosis in the cerebrum. Skeletal changes can occur anywhere in the skeleton and have been described as fibrocystic, cystic, and sclerotic. The diversity and inconstancy of the changes are reflected in the descriptions which have been given by various authors. Since the skeleton is of mesodermic origin, the changes may be as diffuse as they appear to be in the brain. The main changes can be described as being a sclerotic bone change associated with the presence of small cysts in the terminal phalanges. Patchy areas of increased density have been observed in the bones of the skull. It has been suggested that these are related to the underlying tuberous nodules. The picture is quite distinctive and presents a mottled sclerotic appearance of the bone. This is perhaps the most constant finding.

The Roentgen Appearance of Gastric Argentaffinoma. R. Pochaczevsky and R. S. Sherman. Radiology 72:330-337 (March) 1959 [Syracuse, N. Y.].

The authors report 4 patients with gastric argentaffinoma, ranging in age from 42 to 67 years. The first patient had a malignant argentaffinoma, primary in the stomach, with hepatic and ovarian metastases presenting a Krukenberg-like picture. Following total hysterectomy, oophorectomy, and subtotal gastrectomy, the patient has been observed for more than 5 years and is almost completely asymptomatic. The second patient is probably the first with primary gastric argentaffinoma in whom metastases to the bone were found. There were also hepatic, lymph node, and brain metastases. His death was directly due to the disease. The third patient had multiple malignant argentaffinomas of the lower ileum presenting a carcinoid syndrome with extensive metastases, associated with an extrinsic pressure type of defect due to metastases in the fundus of the stomach. A valvular pulmonary stenosis was also present. The fourth patient presented a polypoid carcinoid of the stomach, manifesting few symptoms.

A review of the reports on patients with gastric argentaffinoma in the literature and the authors' own experience showed that the roentgenologic findings are variable and nonspecific. In none of the patients studied was a correct diagnosis made on the roentgenologic appearance alone. Argentaffinoma, although a rare tumor, should be considered in the differential diagnosis of polypoid filling defects of the stomach, particularly in patients with a long history of gastric disease, whose symptoms are suggestive of a carcinoid syndrome. A purely gastric infiltrative defect, demonstrated by roentgenograms, is apparently never caused by gastric argentaffinoma.

Marrow Treatment of Irradiated Dogs. K. A. Parter and N. P. Couch. Brit. J. Exper. Path. 40:52-56 (Feb.) 1959 [London].

Treatment with intravenous homologous bone marrow protects mice, rats, hamsters, and rabbits against the lethal effects of total-body roentgen irradiation during the early postirradiation period. Similar treatment of irradiated dogs did not meet with the same success. Use in the latter study of a dose of irradiation in the LD_{50} range may have been a major factor contributing to failure, as it is now known that supralethal doses of radiation are usually necessary to obtain permanent marrow homotransplants. The experiments described in this paper were concerned with the influence of the dose of radiation on the success of marrow homotransplantation. Male mongrel dogs, weighing 7 to 9.4 kg., were used as recipient animals. They were exposed to whole-body roentgen irradiation. The marrow for postirradiation injection was obtained from female mongrel puppies. The donors were killed, and the marrow from all 8 long limb bones was removed and gently agitated in cold isotonic sodium chloride solution. The suspension was pressed through a nylon filter to exclude coarse bone spicules and then centrifuged to remove the fat. The residue was made up to 30 ml. by adding further isotonic sodium chloride solution and gently mixing. Nucleated cell counts were made on every sample, and each dog received an average of $3,250 \times 10^6$ cells. The marrow suspension was given into a leg vein 1 to 3 hours after irradiation. A contratest group of irradiated dogs were each given 30 ml. of isotonic sodium chloride solution intravenously.

Total and differential leukocyte counts, platelet counts, and hemoglobin and microhematocrit determinations were carried out every 2 days, and neutrophils bearing nuclear "drumsticks" characteristic of the female were sought in stained films. A total of 37 dogs was studied. They were divided into 5 groups. Group 1 were contrastest animals given 450 r total-body irradiation but no bone marrow ($LD_{50}/30$ days = 315 r). Groups 2, 3, 4, and 5 received 450 r, 500 r, 600 r, and 700 r irradiation, respectively, followed by homologous bone marrow treatment. All animals in group 1 (450 r; no marrow) succumbed within 18 days. Temporary transplants of donor marrow and survival of the recipient were observed in 12.5% of the animals after 450 r and in 37.5% after 500 r ($LD_{50}/30$ days = 315 r). Although there was evidence of an initially successful marrow homograft in 50% of the dogs exposed to 600 r and in 40% of those receiving 700 r, early death from intestinal damage occurred in all. No permanent marrow transplants were achieved. There was evidence that the irradiation briefly suppressed the immune mechanism sufficiently to allow the foreign cells to colonize the depleted host marrow spaces, but, when the recipient's ability to respond returned, the transplant was destroyed. Such host rejection of the graft is often seen after sublethal irradiation and may result in a higher mortality in the marrow-treated animals than in those exposed to irradiation alone.

Roentgen Diagnosis of Cancer of Body of Stomach. C. E. Lampe. Ugesk. læger 121:275-279 (Feb. 19) 1959 (In Danish) [Copenhagen].

The material consists of 195 verified cases of cancer of the body of the stomach. On the first roentgen-ray examination after the onset of symptoms which suggested cancer, the diagnosis of cancer was definitely established in 119 cases, changes considered indicative of cancer were observed in 23 cases, and in 53 cases cancer was not demonstrated or was misinterpreted or overlooked. The 41 cases in which niches were present were compared with 54 cases of verified benign niches of the body of the stomach. A regular conical niche suggests benignancy and an irregular flat niche malignancy, but these criteria are not certain. In the individual case it is impossible to determine roentgenologically whether a niche is due to a benign or a malignant lesion.

An Evaluation of the Roentgen Changes in Acute Pancreatitis: Correlation with Clinical Findings. G. N. Stein, M. H. Kalser, N. N. Sarian and A. Finkelstein. Gastroenterology 36:354-361 (March) 1959 [Baltimore].

This report is based on the roentgen-ray studies of 66 patients, with 73 separate admissions to the Graduate Hospital of the University of Pennsylvania, Philadelphia, for an episode of acute pancreatitis. The criteria for diagnosis as well as the pathological classification had been reported before. The significant findings in the survey films of the abdomen were (*a*) the presence of a "sentinel loop" and (*b*) pancreatic calculi or calcifications. The "sentinel loop" of pancreatitis was considered to be an abnormally gas-distended loop (or loops) of small intestine in the left midabdomen or extending into the left upper abdomen and occasionally crossing the midline to the right. This sign occurred frequently; of the 61 survey films made at various times after the onset of symptoms, 34 had one or more air-filled small intestine loops which measured more than 3 cm. in diameter. Ten other patients had air-filled jejunal loops, but the maximal diameter was less than 3 cm. Hence, they were judged to be within normal limits. The incidence of abnormally dilated, air-filled small intestine loops was slightly higher in the group of patients with pancreatitis secondary to alcohol ingestion than in those with concomitant biliary tract disease, but no correlation could be established between the degree of intestinal distention and the serum enzyme values. "Sentinel loops" were encountered in 8 of 9 patients with proved edematous pancreatitis but in only 10 of 21 patients with the necrotizing form of pancreatitis. This was contrary to the anticipated findings. *It would seem that distention of the small* intestine is more likely to occur in the less severe (edematous) pancreatitis than in the fulminating (necrotizing) type.

Pancreatic calcifications or calculi were observed in 10 of the 61 survey films. Although they occurred in a relatively small percentage of patients, when they did occur, they were important for the diagnosis of pancreatitis. Indistinctness or nonvisualization of the psoas muscle shadow was considered of no value, since it is nonspecific and was noted in only 17 of the 61 survey films. Five of the 17 exhibited changes involving the left psoas muscle shadow alone; 7 others had bilateral changes.

The impression of an enlarged papilla of Vater on the descending duodenum (papillary sign) was noted in about 25% of the patients who had barium meal studies. This is an important but not a pathognomonic sign, since it can be seen occasionally in patients with no clinical evidence of pancreatitis. Other abnormalities noted in the survey films of the abdomen occurred too infrequently or were too nonspecific to be of value. In 40 of the patients roentgenograms of the chest were available for review, but although abnormalities were found in 18 of these, they were not specific and could only be regarded as corroborative evidence.

ANESTHESIA

Observations of a Controlled Surgical Series Treated with Promethazine Before Induction. A. H. Smith. New York J. Med. 59:1024-1029 (March 15) 1959 [New York].

The author studied the sedative and antiemetic effect of promethazine hydrochloride in 3,000 private and ward patients who were operated on between January and August, 1956. The results obtained in a small segment of a test series of 152 patients have been compared with those of 52 contratest patients who were substantially comparable as to age, physical status, and severity of operation.

Eighty-six per cent of the 152 patients received 50 mg. of promethazine, 50 to 75 mg. of meperidine, and 0.4 mg. of scopolamine or atropine intramuscularly one-half to 2 hours before the operation. Some of these patients received all 3 agents in one injection; others were given meperidine and scopolamine or atropine 1½ hours before and promethazine one-half hour before induction. Fourteen per cent of the 152 patients received 50 mg. of promethazine intramuscularly and one injection of 0.4 mg. of scopolamine or atropine, but no meperidine, 1 to 1½ hours before anesthetization. Secobarbital or pentobarbital sodium was administered to most of the 52 contratest patients in standard doses 2 hours before the preoperative analgesic. Two patients received no other preanesthetic medication, and one received 0.4 mg. of atropine. A combination of 50 to 100 mg. of meperidine and 0.4 to 0.6 mg. of scopolamine was administered to 40 patients one-half to 1½ hours before operation. Two patients received 0.4 to 0.6 mg. of scopolamine only one-half hour before operation, and 7 received 10 mg. of morphine sulfate and 0.4 mg. of scopolamine or atropine one-half to 1½ hours before induction.

The preoperative and postoperative condition of the patients treated with promethazine showed considerable improvement compared with the contratest patients. The patients to whom this drug was administered came to the operation room in a calm, relaxed state, yet able to cooperate with instructions as desired. Evidences of depression, typical of sedation with conventional agents, were absent, and induction was easier for both patient and anesthetist. In the postoperative period the patients of the promethazine group were more quiet and manageable and less troubled with nausea and vomiting than the patients of the contratest group. If sedatives or antiemetics appeared necessary while the patients were in the recovery room, the same amount of promethazine was administered as was given before the operation; this resulted in a quick recovery from the depressive effects of anesthesia. The recovery room stay was not prolonged if the amount of anesthetic was carefully regulated with consideration of the potentiating properties of the compound. Postoperative analgesics were not required in as large or as frequent doses as are generally necessary under the conventional regimen.

Promethazine proved to be an excellent choice for patients undergoing cesarean section, as well as for sedation of older patients. It is to be remembered, however, that older patients require smaller doses of promethazine than young vigorous adults. Four deaths occurred within a month of operation; none could be attributed to the medication. Rectal suppositories containing 25 mg. of promethazine are desirable for preanesthetic sedation of children.

Hypothermia in Surgery: Analysis of 98 Clinical Cases. V. K. Saini and R. H. Betts. Indian J. Surg. 20:485-491 (Dec.) 1958 [Madras].

Hypothermia as a means of reducing the risk of surgical intervention and as a potent anesthetic agent was used in 98 patients undergoing open cardiac surgery or operations with local interruption of the circulation at the Christian Medical College Hospital in Vellore, India, between 1956 and 1958. Of the 98 patients, 66 were operated on for tetralogy of Fallot, 6 for pulmonary stenosis, 5 for mitral stenosis, 4 for constrictive pericarditis, 2 for atrial septal defects, 3 for aortic regurgitation, 2 for aneurysm of the thoracic aorta, 2 for exploration of the internal carotid artery, and 8 for portal hypertension. Moderate or partial hypothermia was produced by placing the patient on a precooled hypothermia blanket, obtaining body temperatures in the range of 92 to 88 F (33 to 31 C). Complete hypothermia was produced by cooling blankets and additional bags of ice, obtaining body temperatures in the range of 90 to 86 F (32 to 30 C). In most of the patients operated on, hypothermia was used only as an adjunct, and the authors did not use the very low ranges of hypothermia.

There were 18 operative deaths, but only 4 of these were directly related to hypothermia. Ventricular fibrillation occurred in one patient with mitral stenosis; cardiac arrest occurred in one patient with an atrial septal defect; a particularly distressing bleeding tendency resulted in the death of one patient with constrictive *pericarditis;* and the 4th patient apparently died of an acute acidotic syndrome. It appears that hypothermia offers a safe method of achieving certain distinct benefits in the solution of a variety of surgical problems, and that it decreases the risk of certain operative procedures.

PUBLIC HEALTH

Emotional and Other Selected Characteristics of Cigarette Smokers and Nonsmokers as Related to Epidemiological Studies of Lung Cancer and Other Diseases. A. M. Lilienfeld. J. Nat. Cancer Inst. 22:259-282 (Feb.) 1959 [Washington, D. C.].

One of the objections to interpreting the statistical association of cigarette smoking with lung cancer and other diseases as indicating a causal relationship is that the association may be a result of "self-selection." "Self-selection" means that the unknown factors which cause an individual to smoke are also of etiological importance for lung cancer or other diseases. In 1956 a probability sample of the adult population of Buffalo was interviewed to determine whether cigarette smokers differed from nonsmokers with respect to emotional status and other selected characteristics. From this sample, groups of cigarette smokers and nonsmokers were matched by age, sex, race, and social class. This comparison indicated that smokers differ from nonsmokers in their replies to questions concerning emotional status. Cigarette smokers marry more often, move more frequently, change jobs more often, are hospitalized more often, and participate in more sports than nonsmokers. The parents of nonsmokers are more often foreign born than those of smokers. Similarities between smokers and nonsmokers were also observed. No differences were noted with respect to birthplace, religion, education, present marital status, and proportion of lifetime spent in large cities.

Possible interpretations of these results are discussed, emphasizing their bearing on the statistical association of cigarette smoking with lung cancer and other diseases. In the characteristics studied, the degree of difference between smokers and nonsmokers was not sufficient to account for the high degree of association between cigarette smoking and lung cancer and, therefore, could not influence the causal inference derived from this association, though it might be sufficient to explain the association of cigarette smoking with peptic ulcer and coronary artery disease. Further studies are needed to test these possibilities.

Some Hazards of Athletic Exercise. K. Lloyd. Proc. Roy. Soc. Med. 52:151-157 (March) 1959 [London].

The holding of the 6th British Empire and Commonwealth games at Cardiff, Wales, in the summer of 1958, gave the author the opportunity to study the types of injury arising from track and field athletics, boxing, wrestling, weight lifting, swimming, fencing, rowing, cycling, and lawn bowling. Nine hundred sixty-three male and 159 female athletes participated in the games. In the injury analysis, athletics were subdivided into running, jumping, and throwing as the basic physical actions. The hazards that were observed were divided into muscle and tendon tears and strains, joint sprains and traumatic synovitis, and a group of various lesions comprising contusions, lacerations, abrasions, blisters, and fractures. Of 171 muscle and tendon tears and strains, the largest group were minor muscle lesions, including generalized or localized muscle stiffness and muscle pain. The next most frequent in occurrence were tears of the hamstring and quadriceps muscles, the highest incidence of these lesions (39%) being among runners. There were 136 cases of sprained joints and traumatic synovitis and 85 cases of "various" injuries. Wrestlers had the highest rate for joint sprains and "various" injuries and the second highest rate for muscle strains. These consistently high figures for all types of injury made wrestling easily the most hazardous of the sports. Jumping was next, following the same pattern of a high figure for each injury group. Throwing was the next most hazardous, it being evident that this sport traumatizes the joint ligaments more than the muscles, as also does boxing.

Treatment of these lesions was on generally accepted principles, namely, by the first-aid application of cold and pressure and sometimes limiting movement in order to control further hemorrhage. Once this stage was over, various forms of heat, massage, and graduated movement were employed to aid absorption of effusion. The last stage involved increasing mobilization of the new scar tissue, usually by the resumption of graduated training. For minor joint sprains and more severe sprains in the latter stages of healing, local injections of hydrocortisone proved to be a most effective form of treatment. Of the muscle strains, some responded spectacularly to hydrocortisone injections, some showed partial improvement, and others showed no significant improvement. These results may be explained by the fact that it is exceedingly difficult to inject hydrocortisone at the right point and right depth when the strain is somewhere in the middle of a large muscle belly.

Whatever the particular attributes desirable for a particular sport, they have to be married to a skill, and if skill is not trained at the same rate, then the athlete will be liable to injure his muscles or joints through faulty technique. This is believed to be the basic cause of the vast majority of such injuries. Prevention lies with the athlete and his coach in developing technique and skill at a rate commensurate with physical development.

BOOK REVIEWS

A Textbook of Neurology. By H. Houston Merritt, M.D., Professor of Neurology, Columbia University, New York. Second edition. Cloth. $12.50. Pp. 765, with 182 illustrations. Lea & Febiger, 600 S. Washington Sq., Philadelphia 6, 1959.

Since the publication of the first edition in 1955 this has become one of the standard textbooks in neurology. In four years enough changes have taken place to justify a new edition. The literature has been brought up to date and a realignment of diseases and syndromes achieved. The neurological manifestations of leukemia, purpura, tetany, hepatolenticular degeneration, and familial periodic paralysis have been assigned to the chapter on metabolic diseases; the paroxysmal disorders are brought together in one section; and the dystrophies, myotonia, and myasthenia gravis are included in the group of degenerative and heredodegenerative diseases. Newly described diseases have been added and the comments on pathogenesis and therapy expanded. Conditions that seem to the author of less importance than formerly have been condensed and new illustrations added. These changes are welcome and make this edition even more valuable than the first.

Lectures on Epilepsy. Edited by A. M. Lorentz de Haas, Medical Director of Epilepsy Centre, "Meer en Bosch," Heemstede, Netherlands. Published under auspices of Netherlands Society of Psychiatry and Neurology as supplement no. 4 to journal *Folia psychiatrica, neurologica et neurochirurgica neerlandica.* Cloth. $4.75. Pp. 172, with 9 illustrations. Elsevier Press, Inc., Bank of Southwest Building, Houston 2; 110 Supistraat, Amsterdam C, Netherlands; D. Van Nostrand Company, Ltd., 25 Hollinger Rd., Toronto 16, Canada; 358 Kensington High St., London W. 14, England, 1958.

The first contribution in this book is by D. David and M. B. Dell of Paris. Their subject is the surgical treatment of temporal lobe epilepsy. They question the value of corticography and the excision of a specific cortical lesion, which helps only 33% of patients. They prefer stereotaxic destruction of rhinencephalic structures as the treatment for patients with temporal lobe epilepsy. The other three papers are concerned with psychic, mental, or personality disorders of epileptics. H. Vislie and G. F. Henriksen of Oslo use 26 tables in presenting a statistical study of 162 patients. They correlated the mental status with the IQ, the electroencephalogram, and other evidences of a brain lesion, and they found no evidence that dementia resulted from brain lesions that were secondary to convulsions. Psychic symptoms depended more on the extent than on the site of a lesion.

H. Landolt of Zurich made serial EEG's before, during, and after psychotic episodes in 149 patients with epilepsy or schizophrenia. He distinguished four different conditions, postictal twilight states, petit mal states, psychotic episodes (epileptic mania), and episodes with an increase of electroencephalographic abnormality. In some psychotic epileptics he found that control of seizures led to a worsening of the psychotic condition, and that in these patients a certain amount of electroencephalographic abnormality was beneficial. A. M. Lorentz de Haas and O. Magnus of Holland studied 78 epileptics who had experienced episodes of mental illness. These formed 5% of the institutionalized patients, almost all of them adults. This symposium provides the reader with the observations of several European authors who deal with problems that are of immediate concern to students of the brain and of one of its most interesting disorders.

Hématologie clinique. Par Jean Bernard et Marcel Bessis. Cloth. 14,500 francs. Pp. 526, with 332 illustrations. Masson & Cie, 120 boulevard Saint-Germain, Paris 6e, France, 1958.

The authors are well-known investigators in the field of hematology. This monograph is the outgrowth of an exhibit shown at the International Congress of Hematology in Paris where it was very popular. The characteristic presentation of an exhibit is retained: there are many tables and charts in which the essential features of clinical hematological entities are summarized. This feature has been used effectively to great advantage. The result is economy of space and admirable lucidity of presentation. The whole field of hematology is presented in five sections, the first of which is devoted to general hematology. It includes chapters on the general characteristics of blood, blood cells, hemoglobin and iron, immunohematology, hemostasis, and effects of ionizing radiation. Diseases of the erythrocytes and leukocytes and hemorrhagic diseases are covered in the following sections. The last section deals with diagnostic studies. The colored tables are excellent. Phase and electronic photomicrography have been used judiciously to illustrate new observations which were made possible with these modern techniques. The book can be recommended especially to nonspecialists. The tabular method and the lucidity of presentation enable even those with a limited knowledge of French to understand the text.

These book reviews have been prepared by competent authorities but do not represent the opinions of any medical or other organization unless specifically so stated.

QUESTIONS AND ANSWERS

RENAL FAILURE IN NEWBORN INFANTS

To the Editor:—*Please give advice as to future pregnancies in the following case. The first child of a 20-year-old woman, para 2, was born in August, 1957, weighing 5 lb. (2,268 Gm.); at the age of 2 months the infant was admitted to the hospital with pneumonia, which responded well to antibiotics. When the child was about to be discharged, he suddenly died. Autopsy showed acute nephritis with some adrenal hypoplasia. The second child was born in July, 1958, and weighed 6 lb., 4 oz. (2,835 Gm.). The mother was Rh negative and the father Rh positive, but titers throughout pregnancy were negative. The child appeared to be normal for the first 5 weeks of life and then was admitted to the hospital with convulsions. A diagnosis of pneumonia was given, and in the succeeding 78 days of hospitalization the child was found to have persistent proteinuria, slightly decreased blood calcium level, high circulating eosinophil count, low total protein level, normal erythrocyte count with no erythroblasts, high urine albumin level by direct analysis and by electrophoresis, and high serum cholesterol level. The convulsions were stopped, the pneumonia cured by antibiotics and immune serum, the eosinophil count brought to normal by calcium and cortisone therapy, the protein level brought into balance, and the edema reduced by various methods of protein therapy. Each dose of protein, by whatever method given, produced fever. The child died after 78 days in the hospital. Autopsy showed bilateral hypertrophy of the kidneys associated with nephrosis. No family history of similar occurrences could be obtained. What is the advisability in this family as to further pregnancies?*

R. C. Rowan, M.D., Albion, Mich.

Answer.—Although this is an interesting case, much important information is not given. Were the babies premature? Was the pneumonia caused by a virus or bacteria? Were adrenocortical or pituitary hormones given? Was there any evidence of kidney disease before the acute episodes? Was there any evidence of allergic difficulties? Were blood transfusions given? Genitourinary anomalies occur in 5 to 15% of children and infants. The deaths of these two babies were from different causes, although they were related to the kidneys in both cases. The kidneys may fail as the result of many serious diseases as a terminal phenomenon. These two infants apparently were critically ill. Nothing is mentioned about fluids or electrolytes in the treatment. It is not always easy to keep an infant's fluid and electrolytes in balance. Polycystic disease of the kidney is not uncommon and might account for the phenomena present in these two infants, but nothing was said about it in either autopsy. Bacterial studies are also important, because some tragic staphylococcic infections have occurred in hospitals.

In any event, with no history of such illnesses in either parent—and it is not always easy to obtain this history—this consultant believes the patient should by all means be encouraged to have more children. The mother's emotional status is important; whereas one or two live children would probably solve her problem, the death of another child would, of course, aggravate it. One should not overlook the possibility of poisoning, because infants suck and chew on anything they can get in their mouths. The additional hazard of the Rh factor must be faced, but fortunately many of these patients never have trouble and, if a titer develops or rises rapidly, early delivery with or without exchange transfusion often results in a healthy baby.

CAT SCRATCH DISEASE

To the Editor:—*In a patient with cat scratch disease, if palpable glands seem to be broken down should they be removed?*

Alexander A. Brown, M.D., San Antonio, Texas.

Answer.—In most patients with cat scratch disease, suppuration does not occur and there is spontaneous resolution of the involved nodes. Suppuration is not always evidenced by definite fluctuation, as in pyogenic suppurative lymphadenitis. In general, suppuration is probable in a patient with a combination of such features as fever, a large mass, local redness, increase in surface temperature, tenderness, and no decrease in the size of the mass after several days of observation. In such patients aspiration with an 18-gauge needle should be attempted. If pus can be removed by this means resolution is encouraged. Aspiration may be repeated if necessary. If the nodes become necrotic, a chronic draining sinus may be prevented by surgical removal of the nodes. Since periadenitis is usual in this disease, the surgeon will find that operative removal is not a simple procedure, as pus will have dissected through the capsule of the nodes and produced a mass of matted nodes and necrotic tissue. The usual tissue planes will have been obliterated, and, in the removal of the mass, spurts of pus and blood are frequent. In spite of this, suppurative necrotic nodes should be removed surgically to prevent a persistently draining sinus.

The answers here published have been prepared by competent authorities. They do not, however, represent the opinions of any medical or other organization unless specifically so stated in the reply. Anonymous communications cannot be answered. Every letter must contain the writer's name and address, but these will be omitted on request.

PROLONGED USE OF IODINE

To the Editor:—*Is there any likelihood of iodine toxicity in the following situation? For 30 years a patient has used, twice daily, a cotton swab saturated with a 0.5% solution, in glycerine, of 7% tincture of iodine to paint his gums after cleaning his teeth. He began this practice 30 years ago to cure a severe case of pyorrhea and has continued the treatment daily since that time. Except for slight acne, there are no other symptoms.*

Philip G. Kitchen, M.D., Pocono Lake, Pa.

Answer.—The greatest hazard associated with iodine and its compounds is acute poisoning from ingestion, injection, or skin contact. Manifestations of chronic toxicity are relatively mild. Prolonged ingestion of iodine or administration of iodine compounds may lead to iodism in susceptible persons. The approximate dosage at which iodism occurs cannot be stated because individual susceptibility varies. Irritative phenomena develop in the skin and mucous membranes in the form of various rashes and coryza, headache, conjunctivitis, laryngitis, and bronchitis. Less common are stomatitis, parotitis, and anorexia.

The cutaneous manifestations generally occur somewhat late. They may consist of acne, furuncles, erythema, purpura, urticaria, and vesication, and these may be accompanied by fever. These lesions sometimes resemble gummas. Susceptibility to these irritations varies greatly; they may start a few hours after a relatively small dose is taken or only after the long continued use of large doses. Sometimes the symptoms produced by small doses disappear when the dosage is increased. Most commonly, iodine therapy is continued with little regard to iodism, unless this is unusually severe. Since the patient reported has been using an iodine solution daily for 30 years and the only symptom present is slight acne, it is apparent that he is not highly susceptible.

IDENTIFICATION OF NEWBORN INFANTS

To the Editor:—*What is the best method of positive identification of newborn infants? Some physicians at this hospital believe that footprints are not positive identification.*

M.D., New York.

Answer.—The accepted method for the positive identification of newborn infants should include duplicate items of identification such as tapes or waterproof or oilproof bands which should be firmly affixed immediately after birth to the left wrist and right ankle of the infant. They should be prepared individually by the nursing supervisor and list (1) boy or girl, (2) parents' names, (3) date, (4) time of delivery, and (5) physician's name. These data should be placed in the infant's birth record at the same time. Before the infant is taken to the nursery these identification items should be checked by the nurse in charge and the physician. The nursery nurse should recheck these data on admitting the baby. It is good practice to encourage the mother to check the identification of her baby when it is brought to her for nursing and care. Finally, when the baby is discharged from the hospital these identification data should be rechecked with the mother; the bands can be removed at home. If proper techniques are used, the infant's footprints and palmprints and the mother's fingerprints are of real value in positive identification. In most institutions palmprints are preferred to footprints. It is well to inform parents concerning the methods of identification in use at the hospital.

FAMILIAL PERIODIC PARALYSIS

To the Editor:—*Please give information on the treatment of familial periodic paralysis, including the use of thyroid hormone. A patient's serum potassium level on admission to the hospital was 1.55 mEq. per liter, and an electrocardiogram revealed marked hypopotassemic effects. He is 17 years old and has had episodes of the disease every two or three weeks since the age of 11. Other significant laboratory findings included a protein-bound iodine level of 9.4 mcg.% and a basal metabolic rate of +4%, but there were no symptoms or signs of thyrotoxicosis. His urinary 17-ketosteroid level was normal. The episodes were not relieved by 3 Gm. (40 mEq.) of potassium chloride given rapidly by vein, and they subsided completely only after massive doses of this drug. After two weeks of therapy with 28 Gm. (392 mEq.) of potassium chloride daily, his serum potassium level was about 3.2 mEq. and he had a normal electrocardiogram. He is presently taking 28 Gm. of potassium chloride daily, and this has kept him asymptomatic for six weeks. His serum potassium level remains about 3.1 mEq. His urinary potassium level with this dosage is about three times the normal. Is any other medicament indicated in decreasing his potassium requirements?*

Andrew E. Skladany, M.D., Orion, Ill.

Answer.—While the findings described are compatible with familial periodic paralysis, the possibility of primary aldosteronism or of a potassium-losing nephropathy should be considered. Metabolic studies, including exchangeable sodium and potassium measurements, aldosterone excretion, and determination of the effects of variations in the intake of potassium on electrolyte balances and serum potassium and carbon dioxide combining power values, might better define the nature of the disturbance. With recent advances in knowledge of electrolyte metabolism and adrenal function, it is possible that such studies might reveal a metabolic disturbance that does not precisely fit the older concepts of these syndromes. Once the abnormalities of metabolism are defined, treatment could be planned on a more definitive basis. Until such studies are made, the effects of a diet limited in sodium content with no supplemental potassium might be tried.

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Conn, J. W.; Louis, L. H.; Fajans, S. S.; and Streeten, D. H. P.: Intermittent Aldosteronism in Periodic Paralysis: Dependence of Attacks on Retention of Sodium, and Failure to Induce Attacks by Restriction of Dietary Sodium, Lancet **1**:802-805 (April 20) 1957.

ACETYLENE EXPOSURE

To the Editor:—*Is acetylene toxic? It is piped throughout a fabricating plant, under pressure, and is used for the usual oxygen-acetylene torch cutting of steel. Occasionally such work is done in an enclosed space.*

E. D. Huntington, M.D., Chicago.

Answer.—Acetylene acts as a simple asphyxiant, has little or no irritant effect on mucous surfaces, and may be said to be practically nontoxic. Present commercial grades of acetylene contain almost no impurities. In the past, such impurities as phosphine and hydrogen sulfide were more significant hazards than the acetylene itself. The explosive limits of acetylene are 2.5 to 82% by volume in air. A person would suffer no adverse symptoms from exposure to concentrations in the range of the lower explosive limit. The principal hazard is, therefore, the possibility of explosion.

BEEF ADRENAL IN ALLERGY

To the Editor:—*A recent article in a woman's magazine described beef adrenal extract as being effective in the control of asthma. John W. Tintera, M.D., was quoted as an authority, and his treatment was reported to be based on the theory that all allergy is due to adrenal exhaustion. A mother whose child's asthma has been very hard to control would like to know more about this treatment. Please supply further information.*

M.D., Texas.

Answer.—The physician quoted in the article is a general practitioner, and the endocrine clinic of which he is chief consists of himself and possibly one other part-time physician. Few patients are studied or treated. Dr. Tintera is not a member of the endocrine societies or of any national allergy group. There are many journals to which a physician can submit the results of his studies. These are the channels through which new therapeutic methods should be presented. To the best of this consultant's knowledge, all of Dr. Tintera's publications (written with the aid of a professional feature writer) have appeared in lay journals. His previous publications reported on the same material, which he claims to have used successfully to treat alcoholism. The source of his extract is unknown but, as compared to some of the fine pharmaceutical products already available, would represent a crude mixture. The diet charts listed are similar to those often used in the control of obesity. There is no scientific basis for Dr. Tintera's explanation as to how the absorption of ragweed pollen affects the medulla of the adrenals and no proof that allergic patients possess weak, exhausted adrenals which can be put "at rest" by treatment with an extract of beef adrenals.

UROGENITAL TUBERCULOSIS

To the Editor:—*A patient had a right nephrectomy about 15 years ago because of renal tuberculosis. He now has tuberculosis of the urinary tract, proved by a culture of the urine. What is the accepted method of treatment?*

M.D., New Jersey.

Answer.—It would be wise to study the left renal function by an estimation of the blood urea nitrogen level and an excretory urogram to determine the extent of the structural damage to the kidney by the infection. Guinea pig studies would also be corroborative. Treatment consists of general supportive measures, such as bed rest, adequate diet, and chemotherapy. Dihydrostreptomycin and streptomycin in doses of 0.5 Gm. each are given twice a week intramuscularly, unless contraindicated by a serious aural disease, along with 3 Gm. of aminosalicylic acid orally after meals and at bedtime and 100 mg. of isoniazid three times a day by mouth. This schedule should be continued for a year, allowing the patient to be ambulant, depending on the progress of healing. The kidney should be checked from time to time with excretory urograms. Any secondary pyogenic organisms in the urinary tract should be treated with appropriate drugs.

ACRODYNIA

To the Editor:—*Since the age of 3 months, a 3-year-old girl has had an erythematous rash on her palms and soles. More recently she developed atrophy of her gums and started to lose her teeth. Has any such syndrome been described?*

R. W. Ris, M.D., Madison, Wis.

Answer.—This patient probably has acrodynia or pink disease. Chronic mercury poisoning from teething powders or some other mercury-containing ointment or remedy is usually the cause. The onset is gradual with irritability, photophobia, itching rash on the palms and soles, loss of teeth and hair, sweating, and increased blood pressure. If mercury is found in the urine, the patient should be treated with dimercaprol or edathamil, with or without tolazoline for any hypertension. The itching may be relieved by soothing lotions.

WASHINGTON NEWS

Housing Bill Vetoed . .
Witnesses Testify on Forand Bill . .
Government Employee Health Insurance . .
Automobile Safety Hearings . .
New Air Surgeon General . .

HOUSING BILL TURNED DOWN BY PRESIDENT

President Eisenhower's veto of the over-all housing measure imperiled chances for the provision authorizing construction loan guarantees for proprietary nursing homes. The chief executive rejected the measure on the grounds that it was extravagant and inflationary. He attacked key provisions of the measure, including urban renewal and public housing, but did not mention the noncontroversial nursing home section in his veto message.

Neither the House nor the Senate in approving the 1.4-billion-dollar legislation demonstrated sufficient strength to overcome a veto.

The President's action left it up to the Democratic leadership in Congress to formulate a scaled-down measure to meet White House objections, to try to overcome a veto, or to do nothing. However, the latter approach appeared unlikely in view of the necessity for providing needed authority for basic housing programs, such as the Federal Housing Administration's mortgage guarantee operations during the current fiscal year that started July 1.

Mr. Eisenhower also criticized a provision authorizing a 50-million-dollar revolving fund for direct loans to help private nonprofit corporations construct rental housing for the elderly. He said this need can be met by federal insurance of private loans. He did not mention the increase in direct loan authorizations for interns' and nurses' housing from 25 million dollars to $62,500,000.

The nursing home provision, supported by the A. M. A., authorizes loan guarantees by the FHA of up to 75% of the cost of a proprietary nursing home. It is intended to spur construction of such projects. Should a broad housing bill founder in Congress, there is always the possibility that a separate nursing home provision could be enacted.

FORAND BILL HEARINGS

Hearings were held for one week by the House Ways and Means Committee on the disputed Forand measure, which would broaden Social Security benefits to include health care for the aged.

Testifying in opposition were spokesmen for the American Medical Association and some state medical societies. In addition, many other state societies submitted statements to the committee outlining their stands against the controversial proposal sponsored by Rep. Aime Forand (D., R. I.), second-ranking Democrat on the committee.

Among the scores of witnesses testifying were Arthur S. Flemming, Secretary of Health, Education, and Welfare, and spokesmen for the AFL-CIO. Vigorous opposition to the measure was presented by the American Farm Bureau Federation, the American Society of Internal Medicine, the American Nursing Home Association, the College of American Pathologists, the American Pharmaceutical Association, the American Dental Association, the National Association of Manufacturers, the U. S. Chamber of Commerce, and the American Academy of General Practice, among others.

Speaking for the A. M. A. as a whole on Wednesday, July 15, were Drs. Leonard W. Larson, Chairman of the A. M. A. Board of Trustees, and Frederick C. Swartz, Chairman of the A. M. A. Committee on Aging.

Meanwhile, polls of constituents conducted by lawmakers showed a majority of voters to be against the Forand-type approach to medical problems of the aging. Of 10 polls made so far this session 7 showed the home district voters were opposed to the Forand approach.

AUTOMOBILE SAFETY EMPHASIZED BY A. M. A.

The American Medical Association told Congress that improvement of automobile design and installation of safety equipment promise the greatest possibility for rapid reduction in the highway injury and death toll.

In a letter to Rep. Kenneth Roberts (D., Ala.), chairman of a House commerce subcommittee studying auto safety measures, Dr. F. J. L. Blasingame, A. M. A. Executive Vice-president, wrote, "If it is estimated that the average life of an automobile is ten years it is apparent that a very considerable reduction in the severity of injuries and a marked reduction in fatalities could be accomplished in that time if more attention were devoted to providing safety rather than to increased horsepower, streamlining, color and chrome."

Dr. Blasingame said that there is ample evidence now that clearly indicates the definite values of certain safety features of automobile design, construction, and equipment. "Yet these safety features if available at all, are all too often offered as optional equipment at extra cost," he said.

The main measure before the subcommittee is one sponsored by Representative Roberts that would require certain safety features on all automobiles purchased by the federal government. The aim is to spur automobile makers to include such features on all their automobiles, since the government is a big customer.

In an opening statement the lawmaker said, "I regret to say that there is a certain air of indifference, a 'so what' attitude on the part of many who should be concerned."

Dr. Blasingame proposed as standard equipment anchorage for seat belts; crash padding of the dashboard, roof, and other areas; improved steering wheel and recess post; safety door locks; removal of dangerous knobs and edges, and elimination of dangerous exterior design features.

Witnesses for the automobile industry questioned the need for the Roberts bill and declared they believed the industry itself should tackle safety problems, in general. Because of the rapid rate of developments in the safety field, "We must be sure that we do not specify ourselves into a box and put a premium on the status quo rather than stimulating imaginative innovation," said William F. Sherman, speaking for the Automobile Manufacturers Association.

HEALTH INSURANCE FOR FEDERAL WORKERS ADVANCES

After weeks of delay the Senate Post Office and Civil Service Committee finally approved legislation that would set up for the first time a government-wide program of voluntary health insurance for federal workers. If enacted into law the measure would offer the 2 million civilian US employees and more than 2,700,000 dependents health insurance plans similar to those now provided in many industries, where the employees pay part of the premium costs.

The principle of the bill was endorsed by all affected organizations, including the American Medical Association and the administration, although there were disagreements about some details.

As approved by the committee, the measure calls for the government to pay 50% of the cost of the insurance. The total cost to the government, according to Committee estimates, would run about 145 million dollars a year. This compares with the 105-million-dollar maximum the administration requested.

The measure, almost identical to a bill cleared earlier by a subcommittee, would give the Civil Service Commission a "broad framework" within which to establish a program.

A key provision of the legislation authorizes the CSC to sign contracts for the programs and establish alternative benefits which may include deductible and coinsurance features. In its report on the measure the committee said that it "considers it unwise to tie the Civil Service Commission's hands by specifying dollar maximums or to spell out in detail the specific benefit structures."

Benefits proposed for employees covered would include up to 120 days a year of hospitalization in semiprivate accommodations; surgical benefits equivalent to the "reasonable, necessary, and customary" charges "made to persons with incomes less than those of the one-quarter of federal employees earning the highest incomes"; and benefits equivalent to reasonable charges for in-hospital, outpatient, and other ambulatory medical services. For major medical care, after a deduction of $100, 80% of charges up to $1,500 would be paid for expenses not covered by the above benefits. After $1,500 the insurance would cover 100% of charges, under such conditions as the commission sets forth.

Employees would be allowed to enroll for benefits under any of four types of plans—either one nationwide service benefit program or indemnity plan, national employee organization plans, or group-practice prepayment plans.

Most of the administration's objections to the measure centered on the cost it would entail to the government, which administration officials and Republican committee members said would run higher than the committee estimates. However, objections also were raised to the establishment of an Advisory Council to assist the commission and the creation of a Bureau of Retirement and Insurance within the commission.

Employees already retired would not be eligible for the insurance. The A. M. A. had urged that such persons be allowed to join the program.

AIR SURGEON NAMED

Dr. James L. Goddard, 36-year-old career Public Health Service officer, was appointed to one of the nation's top medical posts—civil air surgeon of the Federal Aviation Agency. Dr. Goddard had served for three years with the U. S. Public Health Service as director of its accident prevention program.

In his new position he will be responsible for the physical and mental health requirements for pilots as well as for the nation's air traffic controllers. The post has been filled on an acting basis by Dr. John E. Smith, since the FAA was created in January. Dr. Smith was named chief of the agency's research requirements division.

Dr. Goddard, appointed by FAA Administrator Elwood R. Quesada, is a graduate of George Washington University School of Medicine and received a master of public health degree from Harvard University. He served with the Army Medical Corps during World War II.

PUBLIC HEALTH LEGISLATION CLEARED

Congress approved a five-year extension of current programs of federal aid for training of professional public health personnel and advanced training of professional nurses. The legislation was endorsed by the administration. Congress has not taken action yet on proposed new federal public health programs that the administration had opposed in testimony earlier this year. The disputed programs would have provided construction grants to public health schools and authorized a five-year program, "with such sums as congress may determine," to cover the costs of traineeships for graduate or special training in public health. The administration had contended that these did not contain adequate safeguards that the money would not replace existing sources of financial support.

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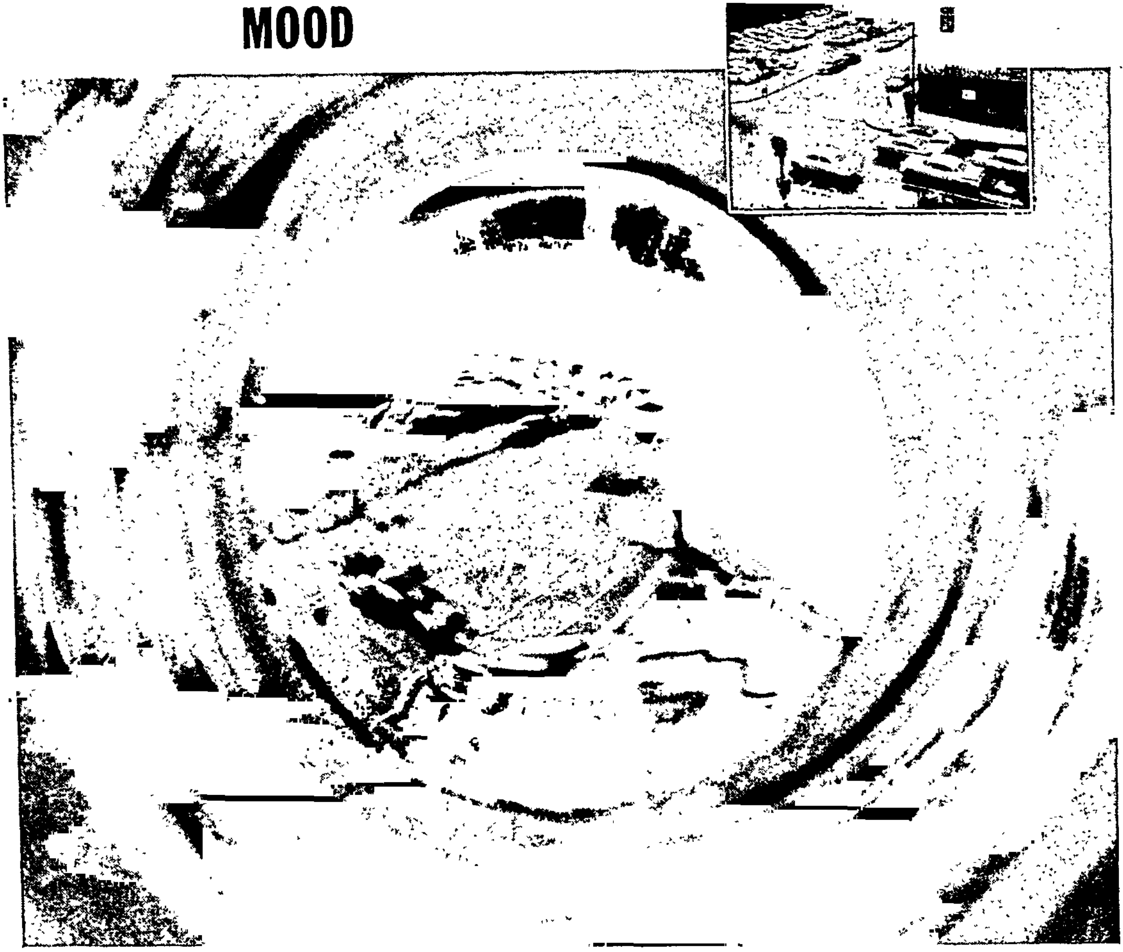

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*Pratt, R. T. C., and McKenzie, W.: Anxiety States Following Vestibular Disorders, Lancet 2:347 (Aug. 16) 1958.

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MEETINGS

AMERICAN MEDICAL ASSOCIATION: Dr. F. J. L. Blasingame, 535 North Dearborn St., Chicago 10, Executive Vice-President.
1959 Clinical Meeting, Dallas, Texas, Dec. 1-4.
1960 Annual Meeting, Miami Beach, Fla., June 13-17.
1960 Clinical Meeting, Washington, D. C., Nov. 29-Dec. 2.
1961 Annual Meeting, New York City, June 26-30.
1961 Clinical Meeting, Denver, Nov. 28-Dec. 1.
1962 Annual Meeting, Chicago, June 13-17.

AMERICAN

1959

July

Rocky Mountain Cancer Conference, Brown Palace Hotel, Denver, July 22-23. Dr. N. Paul Isbell, 835 Republic Bldg., Denver 2, Chairman.

August

American Congress of Physical Medicine and Rehabilitation, Hotel Leamington, Minneapolis, Aug. 30-Sept. 4. Miss Dorothea C. Augustin, 30 N. Michigan Ave., Chicago 2, Executive Secretary.

American Dietetic Association, Statler Hilton, Los Angeles, Aug. 25-28. Miss Ruth M. Yakel, 620 N. Michigan Ave., Chicago 11, Executive Secretary.

American Hospital Association, Statler Hotel, New York City, Aug. 24-27. Dr. Edwin L. Crosby, 18 E. Division St., Chicago, Director and Secretary.

American Veterinary Medical Association, Hotel Muehlebach, Kansas City, Mo., Aug. 24-28. H. E. Kingman Jr., D.V.M., 600 S. Michigan Ave., Chicago 5, Executive Secretary.

Biological Photographic Association, Inc., Sheraton-Mount Royal Hotel, Montreal, Canada, Aug. 31-Sept. 3. Miss Jane H. Waters, Box 1668, Grand Central P. O., New York 17, Executive Secretary.

National Medical Association, Detroit, Aug. 10-13. Dr. John T. Givens, 1108 Church St., Norfolk, Va., Secretary.

Nevada State Medical Association, Reno, Aug. 19-22. Dr. Gilbert G. Lenz, 505 S. Arlington Ave., Reno, Nev., Chairman.

Northwest Proctologic Society, Timberline Lodge, Mount Hood, Ore., Aug. 26-29. Dr. John L. McKay, 645 Medical Dental Bldg., Seattle 1, Secretary-Treasurer.

Rocky Mountain Radiological Society, Shirley-Savoy Hotel, Denver, Aug. 20-22. Dr. John H. Freed, 4200 E. Ninth Ave., Denver 20, Secretary-Treasurer.

Society for Clinical and Experimental Hypnosis, Fairmont Hotel, San Francisco, Aug. 3-5. Dr. Irving Schwartz, 2340 Sutter St., San Francisco 15, Chairman, Program Committee.

Southeastern Oklahoma Clinical Symposium, McAlester Clinic, McAlester, Aug. 8-9. Mr. Charles A. Miller, McAlester Clinic, McAlester, Okla., Business Manager.

West Virginia State Medical Association, The Greenbrier, White Sulphur Springs, Aug. 20-22. Mr. Charles Lively, P. O. Box 1031, Charleston 24, Executive Secretary.

September

American Association of Medical Clinics, Sheraton-Blackstone Hotel, Chicago, Sept. 24-26. Dr. Edwin P. Jordan, Box 58, Charlottesville, Va., Executive Secretary.

American Association of Obstetricians and Gynecologists, The Homestead, Hot Springs, Va., Sept. 10-12. Dr. E. Stewart Taylor, 4200 E. Ninth Ave., Denver 20, Secretary.

American Association for the Surgery of Trauma, Mount Washington Hotel, Bretton Woods, N. H., Sept. 24-26. Dr. William T. Fitts Jr., 3400 Spruce St., Philadelphia 4, Secretary.

American College of Gastroenterology, Biltmore Hotel, Los Angeles, Sept. 19-26. Mr. Daniel Weiss, 33 W. 60th St., New York 23, N. Y., Executive Director.

American College of Surgeons, The Traymore Hotel, Atlantic City, N. J., Sept. 28-Oct. 2. Dr. Paul R. Hawley, 40 E. Erie St., Chicago 11, Director.

American College of Surgeons, Ohio Chapter, Statler Hotel, Cleveland, Sept. 11-12. Dr. Berton M. Bogle, 311 S. Market, Troy, Ohio, Secretary-Treasurer.

American Roentgen Ray Society, The Netherland Hilton Hotel, Cincinnati, Sept. 22-25. Dr. C. Allen Good, Mayo Clinic, Rochester, Minn., Secretary.

American Society of Clinical Pathologists, The Palmer House, Chicago, Sept. 7-11. Mr. Claude E. Wells, 2052 N. Orleans, Chicago 14, Executive Secretary.

Central Association of Obstetricians and Gynecologists, Drake Hotel, Chicago, Sept. 24-26. Dr. Edwin J. DeCosta, 104 S. Michigan Ave., Chicago 3, Secretary.

College of American Pathologists, The Palmer House, Chicago, Sept. 6. Dr. Arthur H. Dearing, Suite 2115, Prudential Plaza, Chicago 1, Executive Director.

Colorado State Medical Society, Brown Palace and Shirley Savoy Hotels, Denver, Sept. 8-11. Mr. Harvey T. Sethman, 835 Republic Bldg., Denver 2, Executive Secretary.

International College of Surgeons, Tennessee Section, Chattanooga, Sept. 28-29. Dr. William G. Stephenson, Medical Arts Bldg., Chattanooga, Tenn., Regent.

Kentucky State Medical Association, Columbia Auditorium, Louisville, Sept. 22-24. Mr. Joseph P. Sanford, 1169 Eastern [illegible] Ky., Executive Secretary.

Maryland, Medical and Chirurgical Faculty of the State of, Semiannual Meeting, Ocean City, Sept. 18. Mr. John Sargeant, 1211 Cathedral St., Baltimore 1, Executive Secretary.

Medical Progress Assembly, Tutwiler Hotel, Birmingham, Ala., Sept. 13-15. Dr. Herbert H. Thomas, 920 S. 19th St., Birmingham, Ala., Chairman, Publicity Committee.

Michigan State Medical Society, Pantlind Hotel, Grand Rapids, Sept. 28-29, Oct. 1-3. Mr. William J. Burns, 606 Townsend St., Lansing 15, Mich., Executive Secretary.

Mid-Continent Psychiatric Association, Holiday Inn Motor Hotel, St. Louis County, Mo., Sept. 18-20. Dr. W. Payton Kolb, Baptist Medical Arts Bldg., Little Rock, Ark., Secretary.

Mississippi Valley Medical Society, Hotel Chase, St. Louis, Sept. 29-Oct. 1. Dr. Harold Swanberg, 209-224 W. C. U. Bldg., Quincy, Ill., Secretary.

Montana Medical Association, Finlen Hotel, Butte, Sept. 17-19. Mr. L. Russell Hegland, 1236 N. 28th St., Billings, Mont., Executive Secretary.

National Recreation Congress, Morrison Hotel, Chicago, Sept. 28-Oct. 2. Mr. Jesse Reynolds, Department of Recreation and Parks, The Mosque, Laurel and Main Streets, Richmond 20, Va., Chairman.

North American Federation, International College of Surgeons, Chicago, Sept. 13-17. For information write the Secretariat, 1516 Lake Shore Dr., Chicago 10.

Ohio Society of Anesthesiologists, Dayton Biltmore Hotel, Dayton, Sept. 18-19. Dr. Nicholas G. DePiero, 9710 Garfield Blvd., Garfield Hts. 25, Ohio, Secretary.

Oregon State Medical Society, Medford Hotel, Medford, Sept. 23-25. Mr. Roscoe K. Miller, 1115 S. W. Taylor St., Portland 5, Ore., Executive Secretary.

Tennessee Valley Medical Assembly, Chattanooga, Tenn., Sept. 28-29. Dr. Guy M. Francis, 109 Medical Arts Bldg., Chattanooga 2, Tenn., Chairman.

United States Section, International College of Surgeons, Palmer House, Chicago, Sept. 13-17. Dr. Ross T. McIntyre, 1516 Lake Shore Dr., Chicago 10, Executive Secretary.

Utah State Medical Association, Hotel Utah Motor Lodge, Salt Lake City, Sept. 16-18. Mr. Harold Bowman, 42 S. 5th East, Salt Lake City 2, Executive Secretary.

Washington State Medical Association, Olympic Hotel, Seattle, Sept. 13-16. Mr. Ralph W. Neill, 1309 Seventh Ave., Seattle 1, Executive Secretary.

World Medical Association, Montreal, Canada, Sept. 7-12. Dr. Louis H. Bauer, 10 Columbus Circle, New York 19, Secretary-General.

October

Academy of Psychosomatic Medicine, Sheraton-Cleveland Hotel, Cleveland, Oct. 15-17. For information write: Dr. Bertram B. Moss, Suite 1035, 55 E. Washington St., Chicago 2, Secretary.

American Academy of Ophthalmology and Otolaryngology, The Palmer House, Chicago, Oct. 11-16. Dr. William L. Benedict, 15 Second St., S. W., Rochester, Minn., Executive Secretary.

American Academy of Pediatrics, The Palmer House, Chicago, Oct. 5-8. Dr. E. H. Christopherson, 1801 Hinman Ave., Evanston, Ill., Executive Secretary.

American Association of Medical Assistants, Benjamin Franklin Hotel, Philadelphia, Oct. 16-18. Mrs. Stella Thurnau, 510 N. Dearborn, Room 924, Chicago 10, Executive Secretary.

American Association of Medical Record Librarians, Radisson Hotel, Minneapolis, Oct. 12-15. Miss Margaret G. Scully, 510 N. Dearborn St., Chicago 10, Director.

American College of Cardiology, Benjamin Franklin Hotel, Philadelphia, Oct. 23-25. Dr. Philip Reichert, Empire State Bldg., New York 1, Executive Director.

American College of Chest Physicians, 25th Anniversary Homecoming Meeting, Albuquerque, N. M., Oct. 14-17. Mr. Murray Kornfeld, 112 E. Chestnut St., Chicago 11, Executive Director.

American College of Preventive Medicine, Hotel Ambassador, Atlantic City, N. J., Oct. 21-22. Dr. John J. Wright, P. O. Box 1267, Chapel Hill, N. C., Secretary-Treasurer.

American Heart Association, Trade and Convention Center, Philadelphia, Oct. 23-27. Mr. William F. McGlone, 44 E. 23rd St., New York 10, Secretary.

American Medical Writers' Association, Chase Hotel, St. Louis, Oct. 2-3. Dr. Harold Swanberg, 510 Maine St., Quincy, Ill., Secretary.

American Otorhinologic Society for Plastic Surgery, Inc., Conrad Hilton Hotel, Chicago, Oct. 11. Dr. Joseph G. Gilbert, 75 Barberry Lane, Roslyn Heights, N. Y., Secretary.

American Psychiatric Association, Detroit Divisional Meeting, Hotel Statler, Detroit, Oct. 29-31. Dr. Benjamin Jeffries, 16321 Mack Ave., Detroit 24, Co-Chairman, Planning Committee.

American Public Health Association, Convention Hall, Atlantic City, N. J., Oct. 19-23. Dr. Berwyn F. Mattison, 1790 Broadway, New York 19, N. Y., Executive Director.

American School Health Association, Claridge Hotel, Atlantic City, N. J., Oct. 18-23. Dr. A. O. DeWeese, 515 E. Main St., Kent, Ohio, Executive Secretary.

American Society of Anesthesiologists, Inc., Americana Hotel, Bal Harbour, Fla., Oct. 5-9. Mr. John W. Andes, 188 W. Randolph St., Room 1101, Chicago 1, Executive Secretary.

American Society of Facial Plastic Surgery, Chicago, Oct. 15-17. Dr. Samuel M. Bloom, 123 E. 83rd St., New York 28, Secretary.

American Society of Plastic and Reconstructive Surgery, Hotel Fountainebleau, Miami Beach, Fla., Oct. 18-23. Dr. Thomas Ray Broadbent, 508 E. South Temple, Salt Lake City, General Secretary.

American Society of Tropical Medicine and Hygiene, Claypool Hotel, Indianapolis, Oct. 28-31. Dr. Rolla B. Hill, 3575 St. Gaudens Road, Miami 33, Fla., Executive Secretary.